Olaparib for maintenance treatment of recurrent, platinum-sensitive ovarian, fallopian tube and peritoneal cancer that has responded to platinum-based chemotherapy

For public - redacted

CDF exit review of TA620

Technology appraisal committee A [13 December 2022]

Chair: Radha Todd

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Company: AstraZeneca

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Appraisal recap

Additional trial data collected since CDF entry will inform committee decision

November 2019
CDF-entry

- Olaparib recommended for 2L use within the CDF (maintenance therapy following 2L chemo)
- 3L use recommended for routine commissioning (met end-of-life criteria)
- OS was based on data from Study 19. Participants were heavily pre-treated and had mixed BRCA status - *"not sufficiently robust to approve for routine commissioning"*
- SOLO2 data more relevant, but OS data was immature at the time

~3 years

December 2022
CDF-review

- OS data from SOLO2 now mature (~40months additional follow-up data, overall maturity [redacted]%).
- Committee to consider whether olaparib is cost-effective in 2L population based on mature SOLO2 data

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2L = second-line; 3L = third-line; BRCAm = BRCA mutation; CDF = Cancer Drugs Fund; OS = overall survival;

Key issues

There are two outstanding key issues, one has a large impact on ICER

Key issues

Issue	Resolved?	ICER impact
Estimation of OS for routine surveillance patients	No	Large ↑↑↑
Costs of subsequent olaparib for routine surveillance patients	No	Small ↓
TTD not capped to PFS	Yes	Small ↓

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ICER = incremental cost-effectiveness ratio; OS = overall survival; PFS = progression free survival; TTD = time to treatment discontinuation;

Background on ovarian cancer

Late diagnosis is common and can lead to poor prognosis

Epidemiology

- 6,300 new ovarian cancer cases in the England every year
- Most cases are in people aged 65yrs+

Diagnosis and classification

- Most common location is the ovary itself (92%), but may be in fallopian tubes or peritoneum
- Classified from stage 1-4, depending on how far it has spread. Majority diagnosed late (stage 3 or 4)
- Also grouped by the type of cell affected and graded depending on how abnormal the cells are
- High-grade serous carcinoma (HGSC) is the most common type of ovarian cancer

Symptoms and prognosis

- Symptoms include pelvic/abdominal pain, bloating, feeling full quickly and urinary frequency/urgency
- High rates of recurrence following initial treatment – risk increases with stage
- Following recurrence, the treatment goal is typically to manage rather than cure the condition
- 5yr survival for ovarian cancer in England is 42.6%; → below the European average

HGSC = High-grade serous carcinoma

Olaparib tablets (Lynparza, AstraZeneca)

Marketing authorisation	Indicated 'as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy'
Mechanism of action	Poly-ADP-ribose polymerase (PARP) inhibitor which inhibits PARP proteins involved in DNA repair. Inhibiting the PARP pathway allows DNA damage to accumulate and limits the options for DNA repair, ultimately resulting in tumour cell death
Administration	Olaparib tablets are taken orally. Dose: 300 mg (2 x 150-mg tablets) taken twice daily (600 mg per day)
Price	List price for tablets is £2,317.50 per 14-day pack (£4,635 per 28-day cycle) A commercial access agreement is in place for olaparib. This arrangement is confidential and will be discussed in part 2 of the meeting.

PARP = Poly-ADP-ribose polymerase

Decision problem

Only appraising 2L maintenance therapy for people with a BRCAm in this CDF exit review

	As per CDF Terms of Engagement
Population	People who have platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube or peritoneal cancer that is in response (complete or partial) to second-line platinum-based chemotherapy, and who have a confirmed BRCAm →*narrower than olaparib marketing authorisation*
Comparators	Routine surveillance
Outcomes	• overall survival • progression-free survival • progression-free survival to second progression • time to next line of therapy • adverse effects of treatment • health-related quality of life

TA620 recommended 3L use for routine commissioning (met end of life criteria), and 2L use in the CDF. Therefore this CDF review is only considering 2L use.

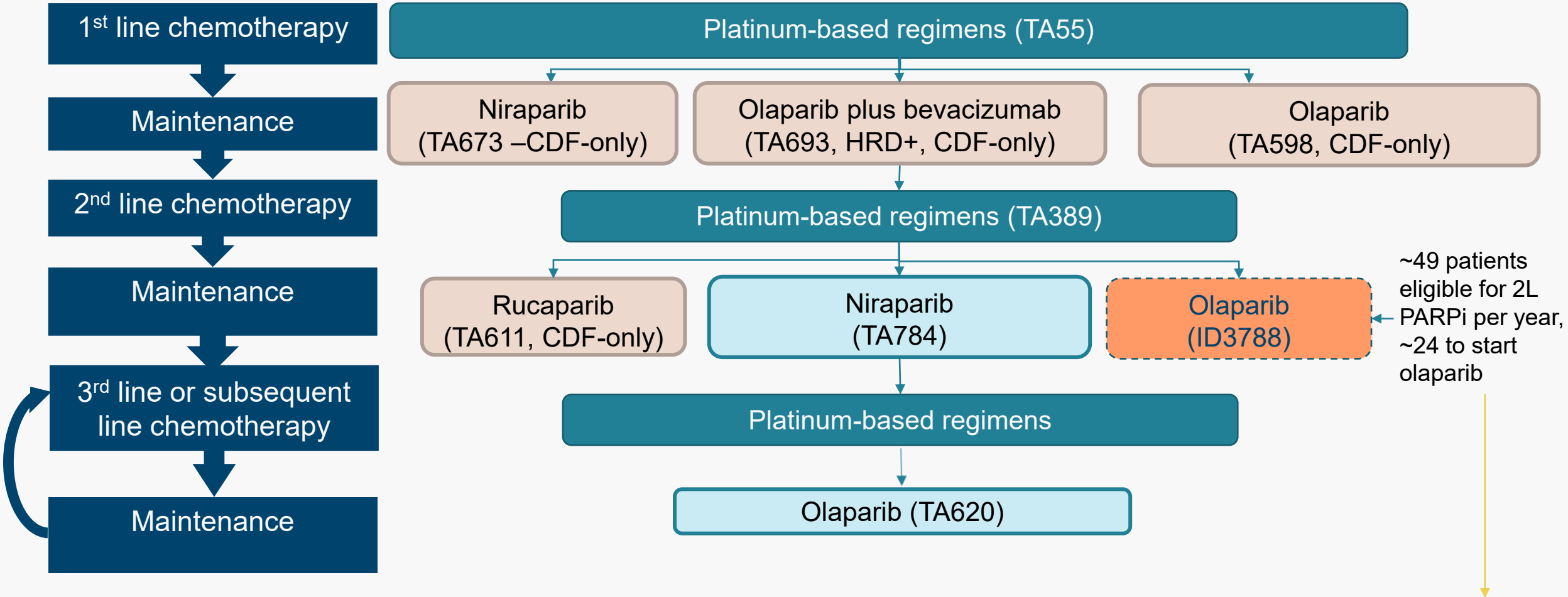
2L = second-line; 3L = third-line; BRCAm = BRCA mutation; CDF = Cancer Drugs Fund

Current Pathway: BRCAm+ Ovarian Cancer

Available in the CDF

In routine commissioning

PARPi now available across all lines but still a need for small minority PARPi naïve at 2L

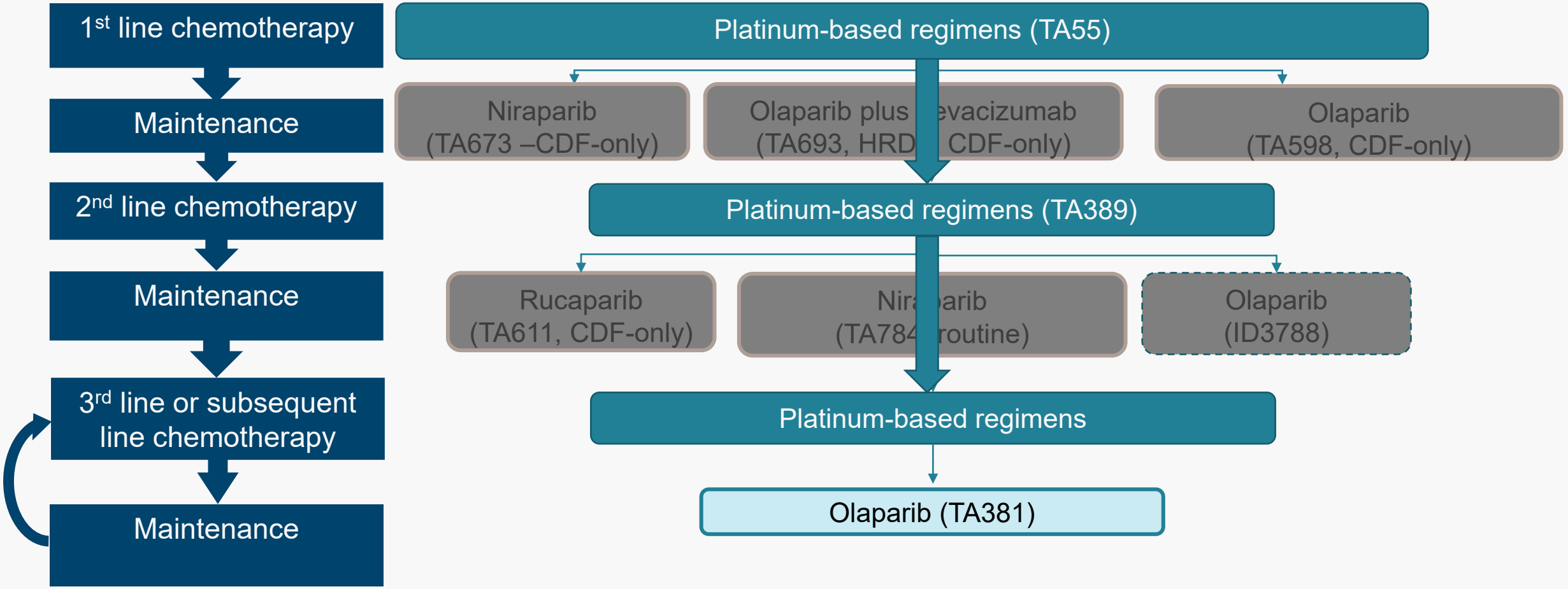


Small number now eligible for olaparib 2L, as most will have PARPi 1L via CDF (*cannot be retreated with PARPi*). However, CDF review needs to consider pathway at time of CDF entry.

2L = second-line; BRCAm = BRCA mutation; CDF = Cancer Drugs Fund; HRD = Homologous recombination deficiency; PARPi = PARP inhibitor

Pathway at the time of CDF entry: BRCAm+ Ovarian Cancer

Olaparib after third line platinum was the only PARP inhibitor in routine commissioning



CDF review needs to consider pathway at time of CDF entry when using this process for exit (no rescope)

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2L = second-line; BRCAm = BRCA mutation; CDF = Cancer Drugs Fund; HRD = Homologous recombination deficiency; PARPi = PARP inhibitor
Olaparib = olaparib tablets, unless otherwise specified

Update since Cancer Drugs Fund entry

ERG says company has adhered to the ToE in general

	Original source	Updated source	ERG comment
Overall survival source	Study 19	SOLO2, adjusted to account for high subsequent PARPi use in placebo arm which would overestimate OS.	Reasonable to adjust for subsequent PARPi use and note exploratory analyses to account for subsequent PARP inhibitor use in the *olaparib* arm
Progression-free survival source	Study 19	SOLO2 using radiological disease progression	Appropriate: Company has used the investigator assessed radiological disease PFS data, with a scenario analysis using BICR-assessed PFS.
Time to treatment discontinuation source	Study 19	SOLO2	Appropriate
Baseline characteristics	Study 19	SOLO2	Appropriately changed to align with source of clinical data
Subsequent treatments	Study 19	SOLO2 final analysis	Appropriately changed to align with source of clinical data
Time horizon	30 years	50 years	Appropriate

BICR = blinded independent central review; PARPi = PARP inhibitor; PFS = Progression Free Survival

Patient perspectives

Olaparib can extend progression-free survival and help people live a normal life

Submissions from Ovacome, Ovarian Cancer Action, Target Ovarian Cancer

- The prospect of recurrence "casts a shadow" over people's lives
- As most people will eventually become platinum resistant, extending PFS is hugely important, both physically and psychologically
- Olaparib has manageable side effects ("*annoying, rather than incapacitating*"). It can be taken at home without the need for hospital visits, and increases the interval between chemotherapy
- People's ability to work or live a normal life are limited by debilitating side effects and the need for regular hospital visits with chemotherapy
- Vital that those who weren't offered a PARPi 1st line have this opportunity at second line. Also vital that there is capacity for BRCA testing for those who weren't tested at diagnosis.
- Continued input from oncology teams offers significant psychological as well as health benefits compared to routine surveillance.

"Fears around recurrence are compounded by the knowledge that there are few treatment options."

"Life for both the patient and carer becomes totally consumed by the disease –hospital appointments, managing side effects, organising childcare, sleepless nights – it's a vicious circle that never seems to end

"Olaparib has transformed my life. It has extended my life by 5 wonderful years. My family and I are forever grateful for this life changing drug. "

PARPi = PARP inhibitor; PFS = Progression Free Survival

Clinical perspectives

Olaparib has become standard care and extends survival

Submissions from Royal College of Pathologists, British Gynaecological Cancer Society and UCL Cancer Institute

- Goal is to delay disease progression, delay the time to further systemic anti-cancer treatment, maintain QoL and prolong survival
- Current standard of care (for platinum-based chemotherapy followed by PARPi maintenance) is universal. No difference in opinion among professionals
- Olaparib is well-tolerated. Side effects are rarely severe and can be readily managed with dose adjustments and supportive medications
- Small proportional of people have exceptional benefit, remaining on olaparib >5 years without further progression (around 20%)
- Olaparib maintenance treatment is also therapeutic for some people, deepening their chemotherapy response
- No significant additional burden is expected on the healthcare system but need sustained adequate funding to determine eligibility for treatment (histopathology and genomic testing)
- Olaparib enables patients to be managed remotely and in the community, minimising hospital attendances

PARPi = PARP inhibitor; QoL = quality of life;

"Maintaining women on outpatient treatment with remote consultations and delaying the need for intravenous chemotherapy has been invaluable"

"Effective targeted therapy with less side effects compared to conventional chemotherapy is a much needed addition."

"Real world studies mirror the benefits seen in clinical trials"

Clinical effectiveness

NICE National Institute for Health and Care Excellence

Key clinical trials

Mature OS data for people with BRCA mutation now available to support CDF review

	Study 19 (used for CDF entry)	SOLO2 (used for CDF review)
Population	Patients with platinum sensitive relapsed ovarian cancer, who are in response to platinum chemotherapy, **irrespective of BRCA mutation status**	Patients with platinum sensitive relapsed ovarian cancer **with BRCA mutation**, who are in response to platinum chemotherapy
Intervention	Olaparib, 400 mg capsules twice daily (N = 136)	Olaparib, 300 mg tablets twice daily (N = 196)
Comparator	Placebo (n=129)	Placebo (n=99)
Outcomes	• Progression-free survival • Time to first subsequent treatment • Time to second subsequent treatment • Overall survival • Health-related quality of life • Adverse events	• Progression-free survival • Progression-free survival to 2nd progression • Time to first subsequent treatment • Time to second subsequent treatment • Overall survival • Health-related quality of life • Adverse events
Median follow-up (OS)	• 6.5 years	• 65.7 months for olaparib • 64.5 months for placebo

Public Health England systemic anti-cancer therapy (SACT) dataset was secondary evidence source but only has [redacted] patients. Due to short data collection time no outcomes were reported, so not included in updated model.

CDF = Cancer Drugs Fund; OS = overall survival;

Baseline characteristics - BRCAm 2L subgroup, SOLO2

Population considered broadly generalisable to NHS

	Olaparib (N=110)	Placebo (N=62)
Age, years		
Mean (SD)	[redacted]	[redacted]
Median (range)	[redacted]	[redacted]
ECOG performance status, n (%)		
0	[redacted]	[redacted]
1	[redacted]	[redacted]
Response to previous platinum therapy, n (%)		
Complete response	[redacted]	[redacted]
Partial response	[redacted]	[redacted]

ERG clinical experts:

- baseline characteristics broadly representative of NHS patients in England
- baseline performance status potentially [redacted] than might be expected

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2L = second-line; BRCAm = BRCA mutation; ERG = Evidence Review Group;

Progression free survival: BRCAm 2L subgroup, SOLO2

Olaparib significantly extends progression free survival in second-line maintenance setting

Investigator-assessed progression-free survival

	Olaparib (N=110)	Placebo (N=62)
Events, n/N (%)	[redacted]	[redacted]
Median time to event, months (95% CI)	[redacted]	[redacted]
PFS benefit, months	[redacted]	
HR (95% CI);	[redacted]	

- Median time to progression benefit of [redacted] months with olaparib vs. placebo
- PFS endpoint was met at primary analysis, so this data is from the primary analysis (Sept. 2016 DCO)

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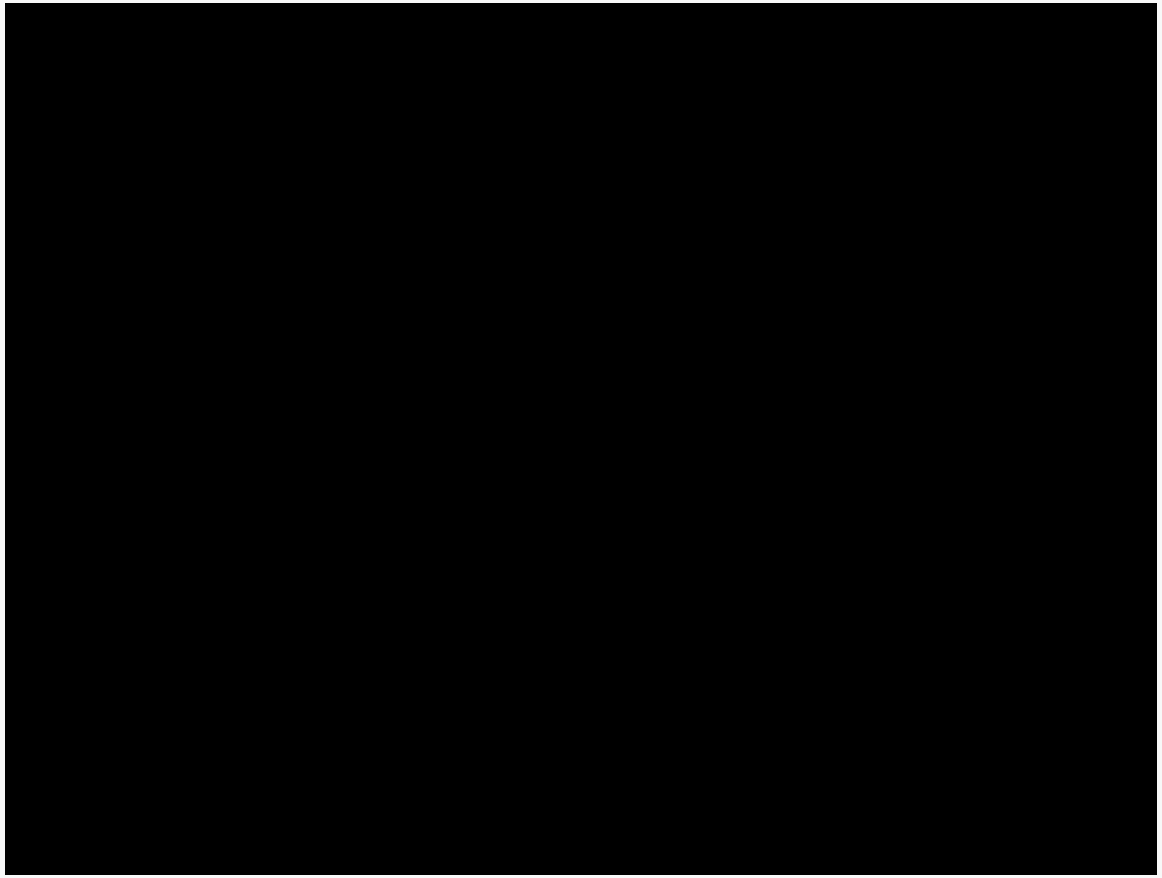
2L = second-line; BRCAm = BRCA mutation; DCO = data cut off; HR = hazard ratio; PFS = progression free survival;

Time to Treatment discontinuation: BRCAm 2L subgroup, SOLO2

Olaparib significantly extends TTD in second-line maintenance setting

Time to treatment discontinuation



	Olaparib (N=110)	Placebo (N=62)
Events, n/N (%)	[redacted]	[redacted]
Median time to event, months (95% CI)	[redacted]	[redacted]
Time to event benefit	[redacted]	
HR primary DCO (Sept 16) (95% CI)	[redacted]	
HR final DCO (95% CI)	[redacted]	

- Olaparib resulted in a median time to event benefit of [redacted] months vs placebo
- TTD data in company submission is from primary analysis (Sept. 2016 DCO).
- Updated HR provided at clarification from final data cut off (Feb 2020)
- ERG said HRs are consistent with each other

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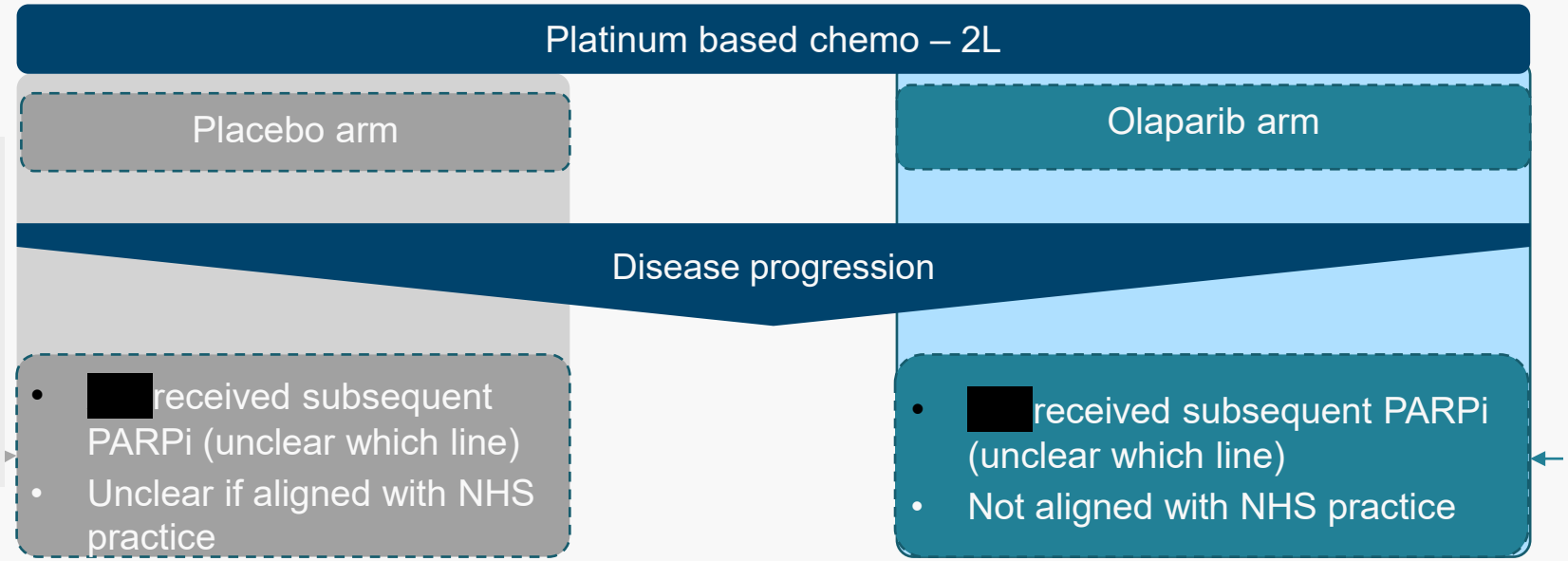
2L = second-line; BRCAm = BRCA mutation; DCO = data cut off; ERG = Evidence Review Group; HR = hazard ratio; TTD = time to treatment discontinuation;

Treatment switching following progression

Company adjusted OS data in placebo arm due to high levels of subsequent PARPi use

People in both arms received subsequent PARPi outside of the study (but higher % in placebo arm)*:

Company applied treatment switching adjustment to the placebo arm, to remove benefit of subsequent PARPi



Company did not apply adjustment to the Olaparib arm as PARPi retreatment had limited impact

Company says adjustment to the placebo arm makes the data generalisable to NHS practice (removing all costs and benefit of subsequent PARPi use). But the ERG feels that *SOME* benefit and cost should be reflected for those eligible for 3L PARPi use in NHS.

Of people who are PARPi naïve at 3L, what % would have olaparib in clinical practice?

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2L = second-line; 3L = third-line; ERG = Evidence Review Group; PARPi = PARP inhibitor; OS = overall survival;
**Subsequent PARPi was taken either as maintenance therapy following platinum-based chemotherapy, or as monotherapy.*

Overall Survival: BRCAm 2L subgroup, SOLO2

Olaparib extends overall survival in second-line maintenance setting

Placebo unadjusted for subsequent PARPi

Placebo adjusted for subsequent PARPi

- Company used rank preserving structural failure time (RPSFT) model to adjust placebo arm
- Adjusted data shows an overall survival benefit of [redacted] months for olaparib vs placebo and [redacted] reduction in mortality risk
- Treatment switching adjustment was pre-specified exploratory analysis

	Unadjusted		Adjusted (with re-censoring)	
	Olaparib (N=110)	Placebo (N=62)	Olaparib (N=110)	Placebo (N=62)
Events, n/N (%)	[redacted]	[redacted]	[redacted]	[redacted]
Median OS, months (95% CI)	[redacted]	[redacted]	[redacted]	[redacted]
OS benefit, months	[redacted]		[redacted]	
HR (95% CI);	[redacted]		[redacted]	

2L = second-line; BRCAm = BRCA mutation; HR = hazard ratio; OS = overall survival; NE = not evaluable; PARPi = PARP inhibitor;

Cost effectiveness

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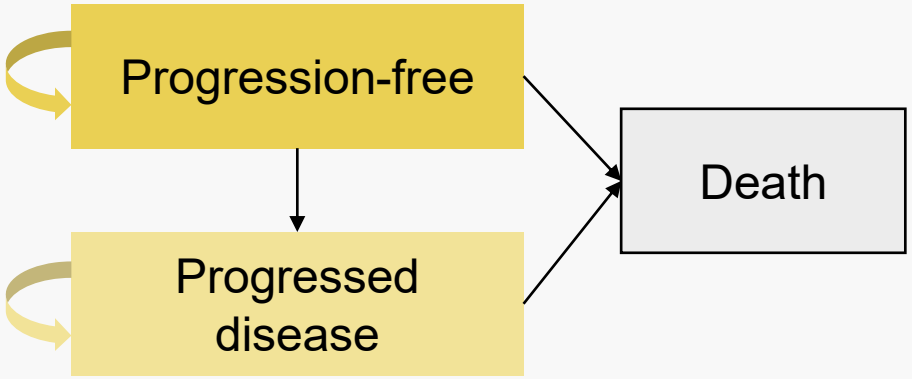
Company's model overview

Model structure same as CDF entry, but different source for clinical data



Model is based on parametric survival curves for

- progression-free survival (PFS)
- overall survival (OS)
- TTD (used to estimate treatment duration)

Area	Assumptions	Aligned with ToE
Population	People with BRCAm after two courses of platinum-based chemotherapy	Y
Time horizon	50 years	Y
Clinical data source	Investigator-assessed PFS, OS and TTD all taken from SOLO2 (as per CDF exit ToE)	Y
Costs	Extrapolation of TTD data from Sept 2016 DCO.	Y
End of life	Not met	Y

BRCAm = BRCA mutation; CDF = Cancer Drugs Fund; DCO = data cut off; OS = overall survival; PFS = progression free survival; TTD = time to treatment discontinuation;

Summary of company and ERG base case assumptions

Two areas remain where ERG and company disagree

Assumptions in company and ERG base case

Assumption	Company base case (post TE)	ERG base case	ICER impact
Adjustment of OS for subsequent PARPi: olaparib arm	No adjustment required		
Adjustment for subsequent PARPi use in RS OS arm (Key issue 1)	Adjusted OS data from SOLO2 with lognormal curve for extrapolation (assumes no 3L PARPi use in RS arm)	Adjusted OS data from SOLO2 with knot spline curve (assumes some benefit from 3L PARPi use in RS arm)	Large
Time-to-treatment discontinuation (TTD) capped to PFS	Capped		
Olaparib 3L costs (Key issue 2)	Omitted	Included	Small

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3L = third-line; ERG = Evidence Review Group; OS = overall survival; PARPi = PARP inhibitor; RS = routine surveillance; TE = technical engagement; TTD = time to treatment discontinuation;

Key issue: Extrapolation of Overall Survival for RS arm

Company and ERG have different approaches for extrapolation of routine surveillance arm

[redacted]

Company

- Selection of lognormal based on statistical goodness-of-fit, visual inspection and external clinical validation

ERG

- Applying lognormal to adjusted data does not capture the survival benefit of 3L olaparib for relapsed RS patients
- Alternative approaches should be considered which reflect this benefit

	Curve selection	3yr survival model	3yr survival SOLO2	20yrs model
Olaparib (unadjusted)	lognormal	[redacted]	[redacted]	[redacted]
Routine surveillance (adjusted)	lognormal	[redacted]	[redacted]	[redacted]

3L = third-line; ERG = Evidence Review Group; RS = routine surveillance

Key issue: Extrapolation of Overall Survival for RS arm - Summary

Company and ERG have different approaches to adjust for high PARPi use in RS arm

No adjustment to <u>olaparib</u> arm required

- Company and ERG both accept that subsequent PARPi use in **olaparib arm** has limited impact and therefore no adjustment is required.

Disagreement over adjustment and/or extrapolation of <u>routine surveillance</u> arm

- Accepted by both company and ERG that some adjustment needs to be made for high use [redacted] of subsequent PARPi in RS arm. Subsequent PARPi was not only olaparib (which it would be in NHS) and not only 3L
- Disagreement over whether the benefit of subsequent PARPi use in RS arm should be removed completely or partially, and which approach should be used to make the adjustment
- Company says 3L+ use of PARPi is diminishingly small, so doesn't need to be reflected in the model
- ERG says at time of CDF-entry, 3L PARPi use was more common, and so does need to be reflected
- ERG's preferred approach to reflect 3L use is to accept the adjustment to the trial data (which removes all benefit), but then chose the extrapolation curve which shows RS arm converging with olaparib arm over time

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3L = third-line; CDF = Cancer Drugs Fund; ERG = Evidence Review Group; PARPi = PARP inhibitor; RS = routine surveillance;

Key issue: Extrapolation of Overall Survival for RS arm – 3L olaparib use

Adjustment does not reflect benefit of 3L olaparib for people in RS arm post-progression

Company

- High rates of subsequent (3L+) PARPi use following progression ([redacted]) inflates survival in the routine surveillance arm. True OS benefit of olaparib likely to be underestimated.
- High subsequent PARPi use also limits generalisability of the data to NHS practice. Negligible number of people now receive PARPi 3L as most now have it 1L or 2L
- Adjustment has been made to OS to remove benefit, but estimate is difficult to externally validate. Retrospective chart review suggests real-world outcomes are worse, so adjusted OS is conservative
- Scenario provided using Study 19 data as subsequent PARPi use was lower than SOLO2 ([redacted] vs [redacted])

ERG:

- Accept that diminishing number of people will now receive PARPi 3L, but some will. Plus, CDF review needs to consider the pathway as it was at CDF entry. So 3L use should be reflected in the model.
- Reasonable to adjust for high subsequent PARPi use, but company's approach may underestimate RS OS
- People in olaparib arm will have no further maintenance treatment options on NHS (only routine surveillance)
- No perfect approach to reflect 3L PARPi use in NHS

Of people who are PARPi naïve at 3L, what % would have olaparib in clinical practice and how is this best reflected in the model?

*_BRCAm_ subgroup only; 1L = first-line; 2L = second-line; 3L = third-line; 3L+ = third-line and later lines; CDF = Cancer Drugs Fund; OS = overall survival; PARPi = PARP inhibitor; RS = routine surveillance

Key issue: Extrapolation of Overall Survival for RS arm – 3L vs 2L benefit

ERG and company disagree on long-term impact of treatment sequencing

ERG:

- Expert opinion and SOLO2 data suggest that the relative survival benefit of olaparib over RS will be similar when given at 3L vs 2L (when PARPi naïve)

Company:

- Relative benefit of olaparib over RS will be similar when given at 3L vs 2L, but there will be differences in prognostic factors at 3L, such as age, residual disease and performance status
- Also more likely to be platinum resistant (so ineligible for targeted maintenance therapy)
- Clinical data and expert feedback indicate the greatest benefit from PARPi is derived from the earlier settings. Unlikely that survival outcomes would be similar in the 2L vs 3L

Clinical experts:

- SOLO1 strongly suggests PARPi gives greatest clinical benefit when used early in pathway
- Likely that 2L use will have a more prolonged effect on survival than 3L use
- "Possible but unlikely" that OS arms would converge
- Fewer people eligible for PARPi by 3L, as more likely to be platinum resistant by this point

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Is it reasonable to assume that people who have PARPi 3L will have similar long-term survival to people who have it 2L?

2L = second-line; 3L = third-line; PARPi = PARP inhibitor; RS = routine surveillance;

Key issue: Extrapolation of Overall Survival in RS arm – 1-knot spline

ERG base case assumes olaparib and RS arms converge

ERG

- Relative benefit of olaparib is similar when given 3L vs 2L (NOVA and SOLO2), so ERG considers that OS for olaparib and RS arms may converge over time
- 1-knot spline shows convergence and gives plausible OS estimates
- Better statistical fit and visual fit to placebo arm than the lognormal (company base case)
- ERG capped routine surveillance OS so that it couldn't exceed olaparib OS (from yr 18 onwards)
- 1-knot spline a reasonable approach to account for the benefit of 3L olaparib (ERG base case)

Company

- 1-knot spline results are clinically implausible based on the data observed in SOLO2. Unlikely that survival outcomes would be similar in the 2L vs 3L (*see previous slide*).
- When validated against company base-case extrapolation, spline underestimates OS for olaparib (~[redacted], vs ~[redacted] for lognormal), but overestimates OS for RS (~[redacted] vs ~[redacted] for lognormal)

2L = second-line; 3L = third-line; ERG = Evidence Review Group; OS = overall survival; RS = routine surveillance;

Key issue: Extrapolation of Overall Survival in RS arm

Methods for OS extrapolation to address switching

Approach	Considerations	5yr OS	
		Olaparib	RS
Adjusted placebo OS with lognormal curve	• Removing the benefit of all subsequent PARPi in the RS arm (which in SOLO2, wasn't limited to 3L olaparib) is consistent with the negligible number of people who would have olaparib 3L.	[redacted]	[redacted]
Adjusted placebo OS with 1 knot spline curve	• Assumes that over time, the OS curves for olaparib and RS may converge. RS patients in the NHS would have 3L olaparib, catching-up with olaparib arm who would have RS.	[redacted]	[redacted]
Apply inverse of unadjusted OS HR to olaparib arm	• Applies the inverse of the unadjusted overall survival (OS) hazard ratio (HR) of [redacted] to the olaparib lognormal OS extrapolation to generate an unadjusted OS curve for RS	[redacted]	[redacted]
Unadjusted OS for olaparib	• Has limitations as assumes that subsequent PARPi use in SOLO2 is all 3L, which it may not be. • Assumes high level of 3L use - not generalisable to NHS	N/R	N/R
Adjusted KM data from SOLO2	*Provided as reference point for validation*	[redacted]	N/R

Company base case

ERG base case

Which adjustment and extrapolation approach best reflects the survival benefit for people in the NHS who will have a PARPi at 3L?

3L = third-line; ERG = Evidence Review Group; KM = Kaplan-Meier; OS = overall survival; PARPi = PARP inhibitor; RS = routine surveillance;

Key issue: Costs of subsequent olaparib for RS arm

Company says costs should only be included if benefits also included

Background

- Original assumptions for TA620 included subsequent olaparib costs for routine surveillance patients
- TTD for 3L patients from TA620/SOLO2 = [redacted] months, updated from final data cut off = [redacted] months

Company

- ERG uses adjusted RS OS data as basis for extrapolation – inconsistent to exclude benefits but include costs
- Costs should only be included where benefits are also included, such as following scenarios:
  - When OS for routine surveillance arm comes from Study 19 (where relatively fewer people received subsequent PARPi than SOLO2, so OS data not adjusted to remove PARPi use)
  - When unadjusted OS is used (so benefit of subsequent PARPi is not removed)
- Negligible number of people now eligible for 3L olaparib *(so excluding costs and benefits of 3L use better reflects current NHS practice)*

ERG comments

- CDF review needs to consider the treatment pathway as it was at CDF entry, despite negligible number of patients now eligible for PARPi at 3L
- Also, relapsed routine surveillance would receive 3L olaparib in NHS and have improved OS
- When using 1-knot spline, the benefits of 3L olaparib are included, so the costs should also be included

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If RS OS is adjusted using 1-knot spline approach (to adjust for 3L olaparib treatment), should the costs of treatment be included?

3L = third-line; CDF = Cancer Drugs Fund; PARPi = PARP inhibitor; RS = routine surveillance; TTD = time to treatment discontinuation;

Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator PAS discounts

- Committee will consider the company and ERG ICERs once confidential comparator PAS discounts are applied
- In general, interventions where the most plausible ICER is less than £20,000 per QALY gained are considered to be cost effective.
- Above this level, committee will take account of the degree of uncertainty around the ICER and the presence of benefits which may not have been adequately captured in the model

ERG = Evidence Review Group; ICER = incremental cost-effectiveness ratio; PAS = patient access scheme; QALY = quality-adjusted life year

Cost-effectiveness results and scenarios

Scenarios applied to company and ERG base cases:

Extrapolation curves

- Weibull to extrapolate TTD - ↓
- Lognormal to extrapolate PFS - ↓
- Log logistic to extrapolate OS - ↑
- Generalised gamma to extrapolate TTD – ↑

Data sources

- Original submission dosage – ↑
- Use BICR-assessed PFS - ↓

Adjustment for 3L olaparib benefit in RS arm

- 1 knot spline OS extrapolation ↑ ↑ ↑
- Inverse of the unadjusted OS HR applied to olaparib OS lognormal extrapolation ↑ ↑ ↑
- Placebo arm OS from Study 19 – ↑ ↑

Olaparib costs

- Include costs of 3L olaparib (TA620 TTD) ↓
- Include costs of 3L olaparib (SOLO2 TTD) ↓

All part 2 ICERs are above the level usually considered as a cost-effective use of NHS resources.

Impact on ICER: ↑ = small; ↑ ↑ = moderate; ↑ ↑ ↑ large.

3L = third-line; BICR = blinded independent central review ICER = incremental cost effectiveness ratio; PFS = progression free survival; TTD = time to treatment discontinuation

Recap of key discussion points

- Of people who are PARPi naïve at 3L, what % would have olaparib in NHS clinical practice?
- Is it reasonable to assume that people who have PARPi 3L will have similar long-term survival to people who have it 2L?
- Which adjustment and extrapolation approach best reflects the survival benefit for people in the NHS who will have a PARPi at 3L?
- If RS OS is adjusted using 1-knot spline approach (to adjust for 3L olaparib treatment), should the costs of treatment be included?

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