Talazoparib with enzalutamide for untreated hormone-relapsed metastatic prostate cancer [ID4004]

PART 1
For screen – contains no confidential information

Technology appraisal committee B [03 December 2025]

Chair: Charles Crawley

External assessment group: Peninsula Technology Assessment Group (PenTAG)

Technical team: Summaya Mohammad, Michelle Green, Mary Hughes, Emily Crowe

Company: Pfizer

Talazoparib with enzalutamide for untreated hormone-relapsed metastatic prostate cancer

- ✓ **Recap**
- ❑ Responses to consultation

NICE National Institute for Health and Care Excellence

Draft guidance recommendation – August 2025

Talazoparib with enzalutamide should not be used for untreated hormone-relapsed metastatic prostate cancer in adults when chemotherapy is not clinically indicated

Why the committee made this recommendation:

- Uncertainty in the indirect treatment comparison of talazoparib plus enzalutamide with abiraterone plus prednisolone and olaparib plus abiraterone and prednisolone
- Uncertainties in the economic model – does not include all usual treatments
- Uncertainties mean it is not possible to determine the most likely cost-effectiveness estimates for talazoparib plus enzalutamide

Consultation comments received from:

- Pfizer (company)
- Stakeholder (Prostate Cancer UK)
- Web comment (clinical expert)

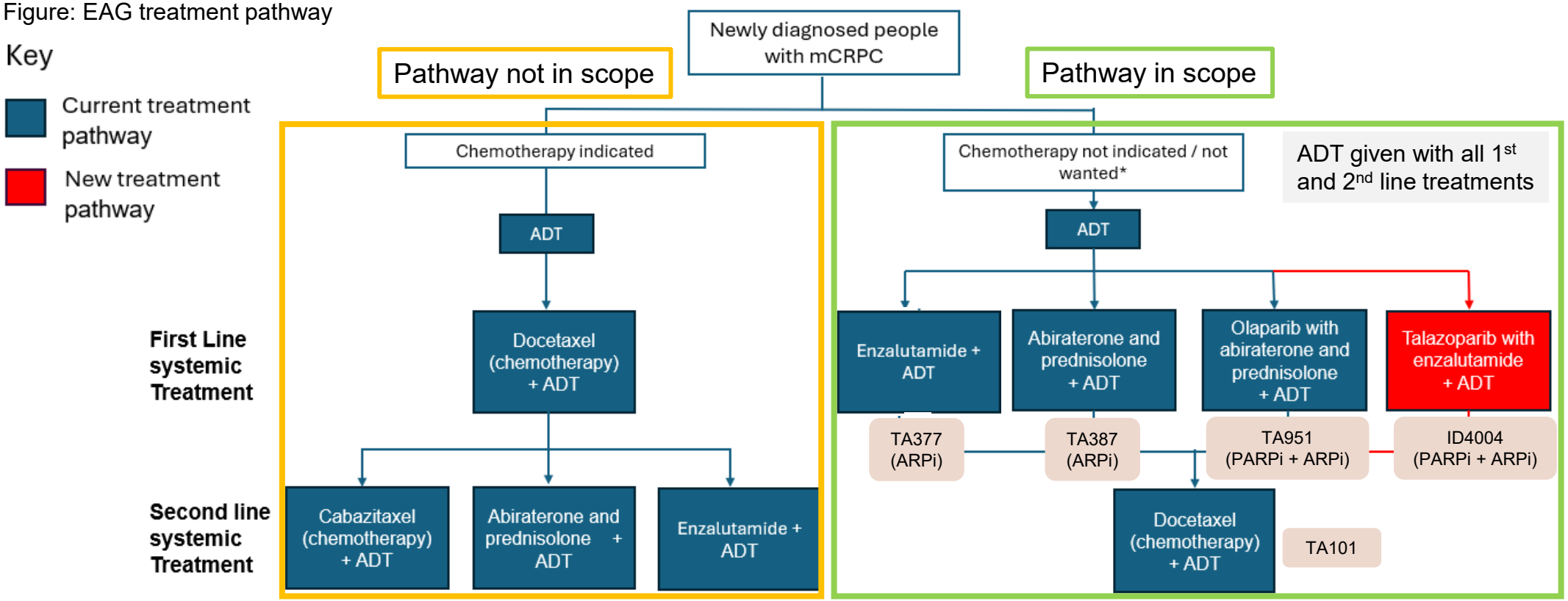
Talazoparib (Talzenna, Pfizer) in combination with enzalutamide (Xtandi, Astellas Pharma)

Marketing authorisation	• Talazoparib "in combination with enzalutamide for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated" • MHRA marketing authorisation issued: 5th July 2024
Mechanism of action	• Talazoparib is a poly adenosine diphosphate-ribose polymerase (PARP) inhibitor – inhibiting PARP1 and PARP2 enzymes, preventing DNA repair • Enzalutamide is a new hormonal agent, inhibiting the androgen receptor pathway (ARPi) • Together, talazoparib and enzalutamide may have a synergistic effect as androgen receptor blockade increases tumour cell sensitivity to PARP inhibition.
Administration	• Oral capsules (talazoparib) / tablets (enzalutamide) • Recommended dose: 0.5 mg talazoparib with 160 mg enzalutamide once daily
List price	• Talazoparib: £1,655.00 per 30 pack of 0.10 mg or 0.25 mg capsules (discount available) • Enzalutamide: £2,734.67 per 112 pack of 40 mg tablets (discount available)

Abbreviations: MHRA: Medicines and Healthcare products Regulatory Agency

Treatment pathway and comparators

Figure: EAG treatment pathway



- Company originally positioned talazoparib with enzalutamide for people with newly diagnosed mCRPC for whom chemotherapy not indicated/not wanted **and in whom olaparib with abiraterone would otherwise be offered**
- EAG: enzalutamide and abiraterone + prednisolone relevant comparators
- Committee conclusion: not possible to define a population in whom abiraterone + prednisolone or enzalutamide would not be an option, and these treatments were relevant comparators.

Abbreviations: ADT – androgen deprivation therapy; ARPi – androgen receptor pathway inhibitor; EAG – external assessment group; PARPi – poly adenosine diphosphate ribose polymerase inhibitor; TA – technology appraisal

ACM1 conclusions for consideration today

Issue	Committee conclusion at ACM1

Treatment pathway and comparators	• Relevant comparators: ABI, ENZ, and OLA+ABI – fully incremental analysis not provided.
	• Requested:
	  • Modelling ABI and ENZ monotherapies as comparators in the same population as OLA+ABI
	  • Fully incremental analyses

Indirect treatment comparison: TALA+ENZ vs ENZ compared in TALAPRO-2 (no direct evidence vs other comparators)	• No suitable indirect treatment comparison approaches • Requested: alternative methods that preserve randomisation, include all the comparators and allow for flexible hazards over time. e.g. multilevel network meta-regressions.
Time on treatment: TTD only available for TALA+ENZ and ENZ monotherapy	• Assume TTD = rPFS for each treatment (for consistency, because TTD not available for all comparators)
Post-progression assumptions and utilities: Company used 0.68 post progression, then 0.5 for palliative care; EAG used single value based on utility estimates from TA951	• Company's post-progression utility values not generalisable to NHS, low palliative care utility value applied for too long • Preferred single value in health state • Request post-progression utility analysis reflecting NHS practice explored

Abbreviations: ABI – abiraterone; ACM – appraisal committee meeting; EAG – external assessment group; ENZ – enzalutamide; NHS – national health service; OLA – olaparib; rPFS – radiographic progression-free survival; TALA – talazoparib; TTD – time to treatment discontinuation

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Draft guidance consultation responses

Company (Pfizer):

- New base case for optimised population where ENZ is only comparator – excludes people eligible for ABI
- Also include fully incremental analysis using PH NMA for indirect comparisons
- Have aligned models to committee's preferred assumptions. Use a midpoint utility value for PD state

Consultation comments – Prostate Cancer UK:

- Concerned people who have fewer treatment options available will miss out on effective treatment
- In practice, many are contraindicated to abiraterone – primary benefit of TALA+ENZ is as alternative and more clinically effective option for those who do not have an ARPi/ alternative PARPi combination
- Urge committee to consider this treatment specifically when contraindicated to abiraterone
- Support decision to assess the treatment beyond HRR-deficient subgroup due to its broader benefits for overall survival and radiographic progression-free survival
- Urge committee to consider this treatment is approved by Scottish Medicines Consortium

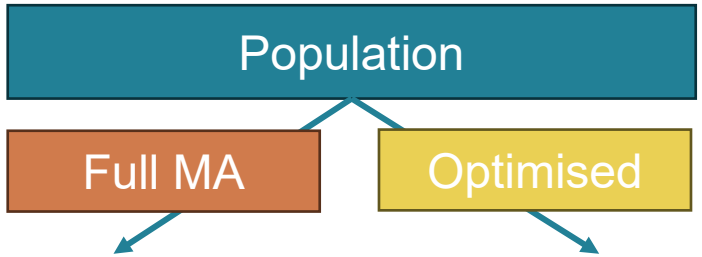
Consultation comments – clinical expert:

- TALA+ENZ is only treatment in first-line castrate resistant prostate cancer to show significant survival benefit
- Should still be considered for selected people who are not eligible for OLA+ABI combination, who would otherwise have enzalutamide

Abbreviations: ABI – abiraterone; ARPi – androgen receptor pathway inhibitor; ENZ – enzalutamide; HRR – Homologous Recombination Repair; NMA – network meta-analysis; OLA – olaparib; PARPi – Poly(ADP-ribose) polymerase inhibitor; PH – proportional hazard; TALA- talazoparib

Summary of cost effectiveness estimates

Considering TALA+ENZ (vs enzalutamide) in an optimised population is the only approach with potential to be cost effective



Issue	Updates for ACM2	Updates for ACM2
Time on treatment	• Company TTD for all treatments except rPFS for OLA+ABI • EAG use DG preferred TTD=rPFS	• TALAPRO-2 TTD data • EAG provide a scenario where TTD=rPFS
Post progression utility	• Company use mid-point 0.7; EAG explore plausible range 0.70 to 0.775	• Company use mid-point 0.7; EAG explore plausible range 0.70 to 0.775
ITC	• No new ITCs, alternative approaches suggested in DG explored but noted unlikely to converge/produce valid results; Company use PH NMA (EAG provide scenario with MAIC for pairwise comparison with OLA)	• N/A TALAPRO-2 trial gives head-to-head data
Cost effectiveness estimates (includes ACM1 committee preferences on costs)	• Both company and EAG preferred assumptions give ICERs above the cost-effective range • N.B. since generics are available, abiraterone is the cheapest option	• Below £30,000

Abbreviations: ABI – abiraterone; DG – draft guidance; EAG – external assessment group; ENZ – enzalutamide; MA – marketing authorisation; MAIC – matching adjusted indirect comparison; NMA – network meta-analysis; OLA – olaparib; PH – proportional hazard; rPFS – radiographic progression-free survival; TALA- talazoparib; TTD – time to treatment discontinuation

Key issue: Treatment pathway and comparators (1/2)

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Company propose optimised population vs enzalutamide monotherapy only

Draft guidance: ABI, ENZ, and OLA+ABI, are all relevant comparators; acknowledge unmet need for first-line treatments and a steroid-free option (ABI always used with prednisolone)

Company response: Propose TALA+ENZ for optimised recommendation in adults **if ABI or ABI-based treatments are unsuitable or not tolerated**

- Clinical and patient expert feedback: Distinct population ineligible for PARPi+ARPi because of co-morbidities that may preclude ABI-based treatment (so ENZ or TALA+ENZ may be preferred)
  - e.g. cardiovascular disease including hypertension, angina, previous myocardial infarction – potential risks of hypertension, hypokalaemia, fluid retention compromising the underlying medical condition
- TALA+ENZ is steroid-free – for those who cannot use steroids long-term, e.g. in diabetes or osteoporosis
- Targeted desktop search for RWE on prevalence of cardiovascular conditions and diabetes in untreated mCRPC: 65.2% cardiovascular conditions; 16.4% diabetes (Chowdhury et al.)
- CPRD (from 2015+): [redacted] adults with prostate cancer and cardiac* or diabetes condition (n=[redacted])

*Cardiovascular disease includes related vascular disorders; co-morbidities captured at any time in medical record

Consultation comments: PCUK: Many contradicted to ABI, so TALA+ENZ is a more clinically effective option for those who would otherwise have ENZ monotherapy – unmet need for ARPi/alternative PARPi

- Clinical expert: People with cardiac history or diabetes are generally preferentially prescribed ENZ rather than ABI + prednisolone – undoubtedly unmet need and would benefit from option of TALA+ENZ

Market share data on proportion having ENZ or ABI at ACM1 (see appendix)

Abbreviations: ABI – abiraterone; ENZ – enzalutamide; OLA – olaparib; mCRPC – metastatic castration-resistant prostate cancer; PARPi: poly adenosine diphosphate ribose polymerase inhibitor; PCUK – Prostate Cancer UK; RWE – real world evidence; TALA- talazoparib

Key issue: Treatment pathway and comparators (2/2)

Summary of cautions in SmPC

EAG critique:

Absolute contraindication to ABI	Relative contraindication to ABI
• Contraindicated for prednisolone • Severe liver impairment (Child-Pugh class C) • Hypersensitivity to ABI or its components	• CVD • Diabetes
EAG clinical experts also agree but note small population	**CVD:** ○ For some people → caution with risks of hypertension, hypokalaemia, fluid retention, recent myocardial infarction, decompensated NYHA III-IV heart failure, uncontrolled hypertension, unstable angina, significant arrhythmia ○ Does not apply to all cardiovascular conditions – poorly controlled CVD is relatively uncommon **Diabetes:** ○ ENZ preferred over ABI (OLA+ABI) to avoid steroids in poorly controlled diabetes – but can be managed

CPRD data: Not limited to mCRPC, or first-line treatment, previous treatment not accounted for, use broad definition of CVD (many eligible for ABI), people contraindicated for prednisolone not included (severe liver impairment or hypersensitivity to ABI) – no meaningful conclusions to draw

Which group of people 1) cannot have ABI and prednisolone? 2) have enzalutamide monotherapy in preference to OLA + ABI? Would people with well managed CVD/diabetes or who have osteoporosis currently have OLA + ABI?

Abbreviations: ABI – abiraterone; CRPD - clinical practice research datalink; CVD – cardiovascular disease; EAG – external assessment group; mCRPC – metastatic castration-resistant prostate cancer; NYHA – New York Heart Association; OLA – Olaparib, SmPC – Summary of product characteristics

Key issue: Time on treatment assumptions

Draft guidance: Committee conclude, assuming TTD=rPFS for each treatment is most plausible option

- TTD data not available for all treatments and no strong justification to assume TTD and rPFS would be different for each treatment

Population	Company approach	Company comment	EAG critique
Optimised	• TALA+ENZ: TALAPRO-2 TTD data • ENZ: TALAPRO-2 TTD data	• Issue not relevant to this population • TALAPRO-2 data consistent approach	Agree with company Scenario for TTD=rPFS provided – relevant if TALAPRO-2 criteria (radiographic progression with no clinical benefit; adverse effects; patient decision; death) not generalisable to NHS

See appendix for Kaplan-Meier, TTD and rPFS

Which approach to modelling time on treatment is preferred?

Abbreviations: ABI – abiraterone; DG – draft guidance; EAG – external assessment group; ENZ – enzalutamide; MA – marketing authorisation; NHS – National Health Service; OLA – olaparib; rPFS – radiographic progression-free survival; TALA – talazoparib; TTD – time to treatment discontinuation

Key issue: Post-progression utility

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Draft guidance:

- Company post-progression utility: 0.658; palliative care utility: 0.5; EAG noted that higher values have been reported in newer literature 0.65 to 0.775. EAG applied 0.775 (TA951) for entire health state
- Committee: Concerned the low palliative care utility value applied for too long, and prefer a single value for full post-progression health state

Company response: Agree using single utility value for full post-progression health state

- Utility value of 0.70 is plausible base case in the middle of the plausible range (0.65 to 0.775)
- Explore alternative scenarios with post-progression including palliative care utilities (0.65 and 0.75)
  - EAG utility is toward higher end of plausible range and may bias against TALA+ENZ

EAG critique: Clarified (reporting in DG) that its previous base case applied multiplier of 0.95 (progression free utility, progressed utility) estimated in PROpel (TA951) to the company estimate for PFS utility from TALAPRO-2 → resulting in utility of [redacted] rather than 0.775 utility (which was progressed disease utility in TA951)

- Now agrees PROpel utility (0.775) is top end of plausible range (relatively close to progression-free values):
  - May reflect stabilisation on subsequent treatments and improved symptom management as people spend more time since progression in the trial;
  - or that people in PROpel who were sicker may be less likely to complete the large number of patient reported outcome questionnaires in that study
- Company's 0.70 is reasonable but plausible range could be between 0.70 and 0.775
- Provide scenarios to explore impact of higher utility values

Abbreviations: EAG – external assessment group; ENZ – enzalutamide; OLA – olaparib; TALA – talazoparib

Which post-progression utility value is most appropriate to use?

Summary of modelling approach – optimised population

Committee ACM1	Company base case	EAG additional scenarios
Efficacy data: ITC including all treatments	• TALA+ENZ: TALAPRO-2 • ENZ: TALAPRO-2	
• OS extrapolations: Gen. gamma • rPFS extrapolations: Gamma But may reassess at ACM2	• TALA+ENZ: Gen. gamma (OS); Gamma (rPFS) • ENZ: Gen. gamma (OS); Gamma (rPFS)	
TTD: assume equal to rPFS for consistency	• TALA+ENZ: TALAPRO-2 TTD data & log-logistic extrapolation • ENZ: TALAPRO-2 TTD data & log-logistic extrapolation	Scenario provided with TTD=rPFS
Post-progression utility: would consider scenarios	0.70 (scenarios using 0.65 and 0.75)	Additional scenario using 0.775
Drug wastage: apply	Fully applied	
End of life costs: exclude	Set to 0	
Skeletal related event costs: exclude and consider as uncaptured benefit	Excluded	

Abbreviations: ACM – appraisal committee meeting; ABI – abiraterone; EAG – external assessment group; ENZ – enzalutamide; Gen. – generalised; HR – hazard ratio; MA – marketing authorisation; NMA – network meta-analysis; OLA – olaparib; OS – overall survival; PH – proportional hazard; rPFS – radiographic progression-free survival; TALA – talazoparib; TTD – time to treatment discontinuation

Other considerations

Equality issues:

- **Draft guidance:** Committee note some people with untreated mCRPC may be older and from a Black African, Black Caribbean, or any other Black or Black British ethnic background. Some people are trans or identify as non-binary. Age, race and gender reassignment are protected under the Equality Act 2010. People from an Ashkenazi Jewish ethnic background have a higher risk of having a BRCA mutation, therefore higher risk of prostate cancer
- No equality issues raised during draft guidance consultation

Managed access:

- Company has not submitted managed access proposal

Uncaptured benefits:

- **Draft guidance:** Cost and disutility associated with skeletal-related events considered as potential uncaptured benefit of TALA+ENZ and should be excluded from base case

Are there any additional equality or uncaptured benefits that are specific to an optimised population?

Abbreviations: BRCA – breast cancer gene; ENZ – enzalutamide; mCRPC – metastatic castration-resistant prostate cancer; TALA – talazoparib

Committee decision making

Key issue	Questions for committee	Impact on ICER (ACM2)
Treatment pathway and comparators	• What is a relevant optimised population to address any unmet need? • Which group of people 1) cannot have ABI and prednisolone? 2) have enzalutamide monotherapy in preference to OLA + ABI?	Large ★★★
Time on treatment	• Which approach to modelling time on treatment is preferred? • Use TTD from trial or use rPFS?	Large ★★★
Post-progression assumption and utilities	• Which post-progression utility value is most appropriate to use? • Midpoint or upper end of plausible range?	Small ★☆☆
Other considerations	• Are there any equality issues or uncaptured benefits to consider?	
Threshold	• What is the committee preferred ICER threshold?	

Abbreviations: ABI – abiraterone; ICER – incremental cost-effectiveness ratio; MA – marketing authorisation; OLA – olaparib; rPFS – radiographic progression-free survival

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Supplementary appendix

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ACM1 conclusions

Issue	Committee conclusion at ACM1	ACM1 ICER impact	Resolved?
Treatment pathway and comparators	• Relevant comparators: Abiraterone, enzalutamide, and olaparib plus abiraterone – fully incremental analysis not provided • Request modelling abiraterone and enzalutamide monotherapies as comparators in the same population as olaparib plus abiraterone	Large ★★★	Partly
Time on treatment	• Assume TTD=rPFS for each treatment	Large ★★★	Partly
Post-progression assumption and utilities	• Company's post-progression utility values not generalisable to NHS • Request post-progression utility analysis reflecting NHS practice	Large ★★★	Partly
Indirect treatment comparison	• No suitable indirect treatment comparison approaches • Request alternative methods that preserve randomisation, include all the comparators and allow for flexible hazards over time. E.g. multilevel network meta-regressions.	Large ★★★	No
Fully incremental analysis	• All comparators included in a single model	Large ★★★	Partly
Enzalutamide OS and rPFS extrapolations	• OS: Generalised gamma; rPFS: Gamma distribution • May need reassessing with updated model for all comparators	Small ★☆☆	Yes
Costs	• Exclude skeletal-related events; an uncaptured benefit • Apply full drug wastage costs; exclude end-of-life care costs; include palliative care costs	Small ★☆☆	Yes

Abbreviations: ACM – appraisal committee meeting; NHS – national health service; OS – overall survival; rPFS – radiographic progression-free survival; TTD – time to treatment discontinuation

Issue applies to both optimised and full MA population

Full MA population ★★★

Optimised population ★★★

Key issue: Time on treatment assumptions

Draft guidance: Committee conclude, assuming TTD=rPFS for each treatment is most plausible option

- TTD data not available for all treatments and no strong justification to assume TTD and rPFS would be different for each treatment

Population	Company approach	Company comment	EAG critique
Optimised	• TALA+ENZ: TALAPRO-2 TTD data • ENZ: TALAPRO-2 TTD data	• Issue not relevant to this population • TALAPRO-2 data consistent approach	Agree with company Scenario for TTD=rPFS provided – relevant if TALAPRO-2 criteria (radiographic progression with no clinical benefit; adverse effects; patient decision; death) not generalisable to NHS
Full MA	• TALA+ENZ and ENZ as per optimised population • OLA+ABI: TTD=rPFS • ABI: TTD = ENZ	Use preferred assumption in DG for OLA+ABI	Company approach is still inconsistent Scenario with TTD = rPFS provided for all treatments

See appendix for Kaplan-Meier, TTD and rPFS

Which approach to modelling time on treatment is preferred?

Abbreviations: ABI – abiraterone; DG – draft guidance; EAG – external assessment group; ENZ – enzalutamide; MA – marketing authorisation; NHS – National Health Service; OLA – olaparib; rPFS – radiographic progression-free survival; TALA – talazoparib; TTD – time to treatment discontinuation

Reliability of indirect treatment comparison from ACM1 (1/2)

Company: Three ITC approaches taken for **TALA+ENZ versus OLA+ABI:** No studies directly compare the treatments – ITC conducted for outcomes of interest including: rPFS, OS

1.Proportional hazard NMA: Assumes hazards are proportional overtime Cox proportional hazards model within a Bayesian framework used

2.Fractional polynomial NMA: Allows for flexible, non-proportional hazard modelling. All OS analyses impacted by non-convergence and could not be used. rPFS fits associated with wide confidence intervals. Estimates considered not usable for modelling.

3.Unanchored MAIC: No common treatment arm, assumes all prognostic factors and effect modifiers included in the analysis and both trial baseline populations are comparable. TALAPRO-2 patient level data matched to PROpel and re-weighted.

Direct treatment comparison for **TALA+ENZ versus ENZ** using TALAPRO-2 trial data provided at clarification

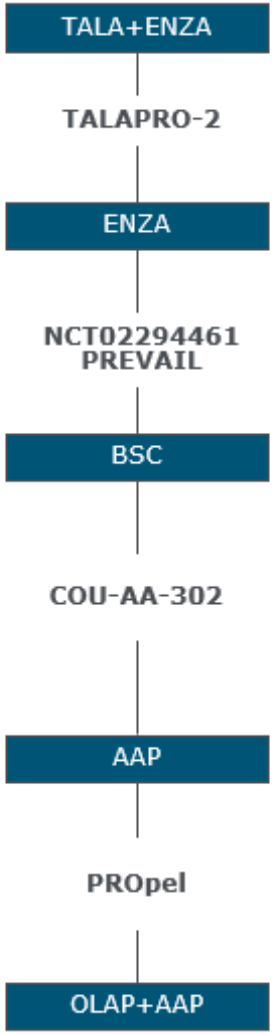

Figure: PH NMA network diagram

Abbreviations: AAP – abiraterone and prednisolone; ABI – abiraterone; ACM – appraisal committee meeting; BSC – best supportive care; ENZ – enzalutamide; ITC – indirect treatment comparison; MAIC – matching adjusted indirect comparison; NMA – network meta-analysis; OLA(P) – olaparib; PH – proportional hazard; rPFS – radiographic progression-free survival; TALA – talazoparib;

Reliability of indirect treatment comparison from ACM 1 (2/2)

Methods	Results (TALA+ENZ vs OLA+ABI)	EAG critique at ACM1	Outcome
PH NMA (company base case at ACM2)	Fixed effects: rPFS: HR [redacted] (95% CrI: [redacted] OS: HR [redacted] (95% CrI [redacted] (Data cutoff: August 2022)	• PH assumption not met for rPFS or OS • Fixed effect analysis preferred • Analysis using August 2022 data cut preferred due to transparency in reporting	Violating PH assumption can lead to biased estimates and inaccurate conclusions – unanchored MAIC & FP NMA requested **Fully incremental analysis possible**
FP NMA	Not applicable	• Uncertainty in rPFS model fits validation • Unable to validate some OS relative effect estimates	OS estimates not usable – MAIC/FP NMA blend needed. FP NMA not suitable for base case. **Fully incremental analysis possible**
Unanchored MAIC – (Company, EAG base case at ACM1)	rPFS: HR: [redacted] (95% CI: [redacted]; p=[redacted] OS: HR: [redacted] (95% CI: [redacted]; p=[redacted] (Data cutoff: September 2024)	• Differences between trial baseline pain score (BPI-SF) could favour TALA • Expert concerned that time to mCRPC was key prognostic factor not adjusted	Results uncertain. No issues with proportionality/ indirectness of evidence. Most appropriate option – company and EAG base case **Robust fully incremental analysis not possible**

Abbreviations: ACM – appraisal committee meeting; CI – confidence interval; CrI – credible interval; EAG – external assessment group; FE – fixed effects; FP – fractional polynomial; HR – hazard ratio; MAIC – matching adjusted indirect comparison; NMA – network meta-analysis; OS – overall survival; PH – proportional hazard; rPFS – radiographic progression-free survival

Issue applies to full MA population

★★★

Key issue: Indirect treatment comparison (1/2)

No further indirect treatment comparison submitted by company

Draft guidance: Committee request analysis that preserve randomisation and model flexible hazards over time to overcome non-proportional hazards issue in NMA, and allow all comparators to be included within 1 analysis

- Suggest alternative approach e.g. multilevel network meta-regressions (ML-NMA)

Company response: Further indirect comparisons not necessary because:

- ENZ is only appropriate comparator – TALAPRO-2 RCT gives head-to-head evidence (TALA+ENZ vs ENZ)
  - Most robust comparative evidence possible for the relevant comparator
  - Maintains randomisation and does not rely on indirect treatment comparisons and population adjustment methods – reduce uncertainty in cost-effectiveness analysis
- Present PH tests for 4 studies in PH NMA used in model – varying results if PH holds (see appendix)
- FP NMA meets committee requirements for indirect treatment comparison allowing all comparators to be included in 1 analysis, preserve randomisation and model flexible hazards over time
- In FP NMA 7 first- and 28 second-order FP models tested:
  - first-order OS had convergency issues or wide CrIs – small network and short OS follow-up
  - first-order rPFS models had some reasonable convergence and CrIs
- No FP model suitable for OS, and 3/35 first- and second-order FP models had appropriate convergence for rPFS – need high quantity and quality of evidence to estimate several complex parameters
- More parameters must be estimated for ML-NMR than in FP NMA, so ML-NMR is unlikely to converge

Abbreviations: CrI – credible interval; ENZ – enzalutamide; FP – fractional polynomial; MA – marketing authorisation; ML-NMR – multi-level network meta-regression; NMA – network meta-analysis; OS – overall survival; PH – proportional hazard; RCT – randomised controlled trial; rPFS – radiographic progression-free survival; TALA- talazoparib

Issue applies to full MA population ★★★

Key issue: Indirect treatment comparison (2/2)

TALA+ENZ vs	ITC model	Difference in mean rPFS (months)	Size of difference in mean rPFS between TALA+ENZ and comparator
ENZ	Proportional hazards NMA	[redacted]	Smallest difference
	MAIC	[redacted]	-
	Fractional polynomial NMA	[redacted]	Greatest difference
OLA+ABI	Proportional hazards NMA	[redacted]	Greatest difference
	MAIC	[redacted]	Smallest difference
	Fractional polynomial NMA	[redacted]	-

Note: Difference in median rPFS by BICR from all-comers population of TALAPRO-2 was [redacted] months [TALA+ENZ: [redacted] months (95%CI: [redacted]); ENZ: [redacted] months (95%CI: [redacted])]

Company: Little difference in impact between alternative ITC methods to estimate relative effects for rPFS (difference in mean rPFS between TALA+ENZ vs ENZ and OLA+ABI)

EAG critique: ITC not needed for optimised population; cannot confirm whether ML-NMR would converge and give valid efficacy results

- Company's assumption using OS and rPFS curves fitted to TALAPRO-2 data in the model does not require proportional hazards assumption – consider this issue to be addressed

- If committee consider the full MA population, are any of the indirect treatment comparisons suitable?
- If committee consider the optimised population, is the company's approach appropriate?

Abbreviations: BICR – blinded independent central reviews; EAG – external assessment group; ENZ – enzalutamide; MA – marketing authorisation; MAIC – matching-adjusted indirect comparison; ML-NMR – multi-level network meta-regression; NMA – network meta-analysis; OS – overall survival; rPFS – radiographic progression-free survival; TALA- talazoparib

Issue applies to full MA population

★★★

Key issue: Fully incremental analysis

Draft guidance: Committee request fully incremental analysis with relative treatment effect derived from indirect treatment comparison including all comparators in a single model

Company response: Consider ENZ as only appropriate comparator for optimised population, but provide fully incremental analysis based on EAG model comparing TALA+ENZA vs OLA+ABI, using:

Comparator	OS and rPFS data source in base case	OS and rPFS data source in scenarios
TALA+ENZ	TALAPRO-2	MAIC for comparison to OLA+ABI
ENZ	TALAPRO-2	-
OLA+ABI	HRs from fixed effects PH NMA applied	• HRs from random effects PH NMA and fractional polynomial NMA (rPFS only) • MAIC for comparison to TALA+ENZ
ABI	Assumed equal to ENZ (differ only in 1st-line drug acquisition costs)	-

EAG critique:

- Agree with company that the revised positioning and population of TALA+ENZ, mean that OLA+ABI and ABI are no longer relevant comparators

- If committee consider the full MA population, is the fully incremental analysis acceptable for decision-making?

Abbreviations: ABI – abiraterone; EAG – external assessment group; ENZ – enzalutamide; HR – hazard ratio; MA – marketing authorisation; MAIC – matching-adjusted indirect comparison; NMA – network meta-analysis; OLA – olaparib; OS – overall survival; PH – proportional hazard; rPFS – radiographic progression-free survival; TALA-talazoparib

Summary of modelling approach – full MA population

Committee ACM1	Company base case	EAG position
Efficacy data: ITC including all treatments	• TALA+ENZ: TALAPRO-2 • ENZ: TALAPRO-2 (assume ABI=ENZ) • OLA+ABI: PH NMA, FE, HRs applied to TALA+ENZ curves	Prefer ITC using unanchored MAIC but acknowledge that this doesn't allow all treatment options in same population. Comparison with ABI is key in this population
• OS extrapolations: Gen. gamma • rPFS extrapolations: Gamma But may reassess at ACM2	• TALA+ENZ: Gen. gamma (OS); Gamma (rPFS) • ENZ: Gen. gamma (OS); Gamma (rPFS) (assume ABI=ENZ) • OLA+ABI: HRs applied to TALA+ENZ curves	TALA+ENZ, ENZ and ABI: company approach is as per EAG's preference at ACM1 OLA+ABI: Gen. gamma (OS); lognormal (rPFS) based on MAIC data
TTD: assume equal to rPFS for consistency	• TALA+ENZ: TALAPRO-2 TTD data & log-logistic extrapolation • ENZ: TALAPRO-2 TTD data & log-logistic extrapolation (assume ABI=ENZ) • OLA+ABI: Assumed equal to rPFS	TALA+ENZ, ENZ and ABI: company approach is as per EAG's preference at ACM1 OLA+ABI: ratio from TALAPRO-2 applied to rPFS (at ACM1) EAG ACM2 base case uses TTD = rPFS for all treatments
Post-progression utility: would consider scenarios	0.70 (plausible range 0.65 to 0.775)	Used multiplier to apply absolute decrease to progression-free utility of [redacted] – approx. 5% decrease in utility. Scenarios provided
Drug wastage: Apply	Fully applied	Company approach is as per EAG's preference at ACM1
End of life costs: Exclude	Set to 0	
Skeletal related event costs: exclude, consider uncaptured benefit	Excluded	

Abbreviations: ACM – appraisal committee meeting; ABI – abiraterone; EAG – external assessment group; ENZ – enzalutamide; Gen. – generalised; HR – hazard ratio; ITC – indirect treatment comparison; MA – marketing authorisation; OLA – olaparib; OS – overall survival; PH – proportional hazard; rPFS – radiographic progression-free survival; TALA – talazoparib; TTD – time to treatment discontinuation

Committee decision making

Key issue	Questions for committee
Treatment pathway and comparators	• What is a relevant optimised population to address any unmet need? • Which group of people 1) cannot have ABI and prednisolone? 2) have enzalutamide monotherapy in preference to OLA + ABI?
Time on treatment	• Which approach to modelling time on treatment is preferred?
Post-progression assumption and utilities	• Which post-progression utility value is most appropriate to use?
Indirect treatment comparison	• If committee consider the full MA population, are any of the indirect treatment comparisons suitable? • If committee consider the optimised population, is the company's approach appropriate?
Fully incremental analysis	• If committee consider the full MA population, is the fully incremental analysis acceptable for decision-making?
Other considerations	• Are there any equality issues or uncaptured benefits to consider?
Threshold	• What is the committee preferred ICER threshold?

Abbreviations: ABI – abiraterone; ICER – incremental cost-effectiveness ratio; MA – marketing authorisation

Summary of contraindications/cautions in SmPC

	ABI+PP	ENZ	TALA (+ ENZ)
Contraindications	Hypersensitivity to active substance/excipients		
	• Severe liver impairment		
Cautions relating to comorbidities	• People with conditions that might be compromised by increases in blood pressure, hypokalaemia, fluid retention • Before treatment hypertension, hypokalaemia and hypertension should be corrected • History of cardiovascular disease (trials excluded people with uncontrolled hypertension, clinically significant heart disease, heart failure NYHA class II to IV, LVEF <50% • People with decreased bone density (ABI+PP can increase this effect) • People with diabetes (corticosteroids can increase blood sugar→ increase monitoring needed)	• Severe liver or kidney impairment • Trials excluded people with recent myocardial infarction, unstable angina, NYHA III or IV heart failure except if LVEF ≥45%, bradycardia or uncontrolled hypertension	Increases risk of • Myelosuppression: should not be used until people have recovered from haematological toxicity from previous treatments • Myelodysplastic syndrome/acute myeloid leukaemia, needs monitoring can lead to stopping treatment • Venous thromboembolic events risk with talazoparib
Cautions relating to medications	• Previous ketoconazole (lower response) • Pioglitazone or repaglinide for diabetes (ABI+PP increases risk of hypoglycaemia)	• Warfarin and coumarin like anticoagulants • Treatments that prolong QT interval	

Abbreviations: ABI – abiraterone; ENZ – enzalutamide; IV – intravenous; LVEF – left ventricular ejection fraction; NYHA – New York Heart Association Functional Classification; OLA – olaparib; PP – prednisolone; SmPC – summary of product characteristics; TALA – talazoparib;

Abiraterone Blueteq criteria

Abiraterone for treating mCRPC before chemotherapy is indicated:

1. This application is being made by and the first cycle of systemic anti-cancer therapy with abiraterone will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.
2. This patient either has a proven histological or cytological diagnosis of adenocarcinoma of the prostate or has presented with a clinical picture consistent with metastatic prostate cancer with both widespread bone metastases radiologically typical of prostate cancer and a serum PSA of ≥50 ng/mL.
3. This patient has hormone-relapsed (castrate-resistant) metastatic prostate cancer.
4. The patient has no or only mild symptoms after androgen deprivation therapy has failed.
5. Chemotherapy is not yet indicated.
6. One of the following applies to this patient as regards any previous use of 2nd generation receptor inhibitors (such as enzalutamide, darolutamide or apalutamide) or CYP17 enzyme inhibitors (such as abiraterone). Please enter below as to which scenario applies to this patient: - the patient has not been previously received any treatment with enzalutamide or darolutamide or apalutamide or abiraterone or - the patient has previously received enzalutamide for this same pre-chemotherapy indication in hormone-relapsed (castrate-resistant) prostate cancer but it was stopped within 3 months of it starting due to dose-limiting toxicity and in the clear absence of disease progression
7. Abiraterone is to be given in combination with prednisolone
8. The patient has an ECOG performance status (PS) of 0 or 1 or 2.
9. Abiraterone is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
10. A formal medical review as to how abiraterone is being tolerated and whether treatment with abiraterone should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
11. Where a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.
12. Abiraterone is to be otherwise used as set out in its Summary of Product Characteristics.

Abbreviations: ECOG – Eastern Cooperative Oncology Group; mCRPC – metastatic castration resistant prostate cancer; ml – millilitre; ng – nanogram; PSA – prostate specific antigen

Enzalutamide Blueteq criteria

Enzalutamide for treating mCRPC before chemotherapy is indicated:

1. This application is being made by and the first cycle of systemic anti-cancer therapy with enzalutamide will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.
2. This patient either has a proven histological or cytological diagnosis of adenocarcinoma of the prostate or has presented with a clinical picture consistent with metastatic prostate cancer with both widespread bone metastases radiologically typical of prostate cancer and a serum PSA of ≥50 ng/mL.
3. This patient has hormone-relapsed (castrate-resistant) metastatic prostate cancer.
4. The patient has no or only mild symptoms after androgen deprivation therapy has failed.
5. Chemotherapy is not yet indicated.
6. One of the following applies to this patient as regards any previous use of 2nd generation receptor inhibitors (such as enzalutamide, darolutamide or apalutamide) or CYP17 enzyme inhibitors (such as abiraterone). Please enter below as to which scenario applies to this patient: - the patient has not been previously received any treatment with enzalutamide or darolutamide or apalutamide or abiraterone or - the patient has previously received abiraterone for this same pre-chemotherapy indication in hormone-relapsed (castrate-resistant) prostate cancer but it was stopped within 3 months of it starting due to dose-limiting toxicity and in the clear absence of disease progression
7. The patient has an ECOG performance status (PS) of 0 or 1 or 2.
8. Enzalutamide is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
9. A formal medical review as to how enzalutamide is being tolerated and whether treatment with enzalutamide should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
10. Where a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.
11. Enzalutamide is to be otherwise used as set out in its Summary of Product Characteristics.

Abbreviations: ECOG – Eastern Cooperative Oncology Group; mCRPC – metastatic castration resistant prostate cancer; ml – millilitre; ng – nanogram; PSA – prostate specific antigen

Olaparib Blueteq criteria

Olaparib with abiraterone for treating mCRPC in people who are treatment naïve to androgen receptor inhibitors and where chemotherapy is not yet clinically indicated or appropriate:

1. This application for olaparib plus abiraterone is being made by and the first cycle of systemic anti-cancer therapy with olaparib plus abiraterone will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.
2. The patient either has a proven histological or cytological diagnosis of adenocarcinoma of the prostate or has presented with a clinical picture consistent with metastatic prostate cancer with both widespread bone metastases typical of prostate cancer and a serum PSA of at least 50ng/ml.
3. The patient has metastatic prostate cancer.
4. The patient has progressive hormone-relapsed (castrate-resistant) disease.
5. The patient has not been treated with chemotherapy for the hormone-relapsed (castrate-resistant) indication and that for this same hormone-relapsed (castrate-resistant) indication chemotherapy is either not yet clinically indicated or is inappropriate (contraindicated or declined by the patient). Note: chemotherapy given for hormone-sensitive disease earlier in the treatment pathway does not exclude patients from potential access to olaparib plus abiraterone.
6. The patient has not previously received any therapy with an androgen receptor inhibitor such as enzalutamide, abiraterone, apalutamide or darolutamide at any place in the prostate cancer treatment pathway except in the case of patients who received androgen receptor inhibitor therapy for hormone-sensitive disease and stopped this treatment more than 12 months prior to this application without PSA progression or evidence of clinical or radiological progressive disease at the time such androgen receptor inhibitor therapy was discontinued. Please mark below which scenario applies to this patient: - the patient has not previously received any therapy with an androgen receptor inhibitor such as enzalutamide, abiraterone, apalutamide or darolutamide at any place in the prostate cancer treatment pathway OR - the patient received androgen receptor inhibitor therapy for hormone-sensitive disease and stopped this treatment more than 12 months prior to this application without PSA progression or evidence of clinical or radiological progressive disease at the time such androgen receptor inhibitor therapy was discontinued.
7. The patient has not received any previous PARP inhibitor therapy unless olaparib has been received for this indication via a company compassionate access scheme in which case all other treatment criteria on this form must be fulfilled.
8. The patient has an ECOG performance score of 0 or 1.
9. Olaparib is only to be given in combination with abiraterone plus prednisolone. Note: olaparib cannot be given in combination with enzalutamide or any other androgen receptor inhibitor. Note: it is expected that treatment with LHRH agonists/antagonists will continue unless the patient has undergone surgical castration.
10. Olaparib and abiraterone are to be continued until disease progression or the development of unacceptable toxicity or patient choice to discontinue treatment, whichever is the sooner.
11. A formal medical review as to how olaparib and abiraterone are being tolerated and whether treatment with olaparib plus abiraterone should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
12. When a treatment break of more than 6 weeks beyond the expected 4-week cycle length is needed, the prescribing clinician will complete a treatment break approval form to restart treatment.
13. Olaparib and abiraterone will otherwise be used as set out in their respective Summaries of Product Characteristics (SPCs).

Abbreviations: ECOG – Eastern Cooperative Oncology Group; mCRPC – metastatic castration resistant prostate cancer; ml – millilitre; ng – nanogram; PSA – prostate specific antigen

Key clinical trial: TALAPRO-2

	TALAPRO-2 (n = 805)
Design	Two-part trial. Part 2 included in company submission and economic model: ongoing randomised, double-blind, placebo-controlled, phase 3 study.
Population	Adults with asymptomatic or mildly symptomatic mCRPC, receiving ongoing ADT, with an Eastern Cooperative Oncology Group performance status (ECOG PS) score of 0 or 1 Cohort 1: including everyone irrespective of homologous recombination repair (HRR) gene alterations Cohort 2: restricted to people with HRR gene alterations Cohort 1 included in company submission and economic model
Intervention	Talazoparib (0.5mg daily) in combination with enzalutamide (160mg daily) (n=402)
Comparator(s)	Placebo in combination with enzalutamide (160mg daily) (n=403)
Primary outcome	Radiographic progression or death (rPFS) by blinded independent central review (BICR)
Key secondary outcomes	Overall survival, rPFS (investigator assessed), objective response rate (investigator assessed and BICR), adverse events, health-related quality of life
Locations	287 sites in 26 countries in North America, Europe, Israel, South America, South Africa, and the Asia-Pacific region
Used in model?	Yes (Cohort 1 only)
Subgroups	Pre-specified subgroup analyses included: age, geographical region, ECOG (0 vs 1), Gleason score, type of progression, baseline PSA, site of metastasis, HRR gene alteration status, previous taxane or novel hormonal therapy

Abbreviations: ADT – androgen deprivation therapy; BICR – blinded independent central review; ECOG PS – Eastern Cooperative Oncology Group performance status; mCRPC – metastatic castration-resistant prostate cancer; HRR – homologous recombination repair, PSA – prostate specific antigen

TALAPRO-2 trial results

	TALA+ENZ (n=402)	ENZ + PBO (n=403)	HR (95% CI)
Median rPFS by BICR, months (95% CI)	33.1 (27.4, 39.0)	19.5 (16.6, 24.7)	0.667 (0.551, 0.807) p-value <0.0001
Median OS (95% CI), months	45.8 (39.4, 50.8)	37.0 (34.1, 40.4)	0.796 (0.661, 0.958) p= 0.0155

Note: Talazoparib and placebo given in combination with enzalutamide. Table adapted from addendum tables 1-2

Figure: Kaplan-Meier plot of BICR-assessed rPFS

Cohort 1 Part 2 all-comers ITT population at final data cutoff 3rd Sept 2024 (N=805):
Compared to placebo with enzalutamide, talazoparib with enzalutamide (TALA+ENZ) shows:

- statistically significant and clinically meaningful improvement in BICR-assessed rPFS
- statistically significant and clinically meaningful improvement in overall survival (OS)

Abbreviations: BICR – Blinded Independent Central Review; CI – confidence interval; ENZ – enzalutamide; HR, hazard ratio; NR, not reported; OS, Overall survival; PBO – placebo; rPFS: radiographic progression-free survival; TALA – talazoparib

Market share data from ACM1

EAG comments:

- **Comparators:** Market share shows 50-56% get ENZ and 31%-38% get ABI

National Clinical Lead for cancer drugs:

- In full indication patient access per year is: 1,350 for ENZ, 700 for ABI, 350 for OLA+ABI (→ OLA+ABI market share taken from mainly those who would have had abiraterone monotherapy and not enzalutamide)

Note: Current market share estimates for mCRPC (Blueteq submissions for last 6 months up to 31 October 2025)

- ENZ: 59.7%
- ABI + ADT + prednisolone: 29%
- OLA+ABI + prednisolone: 11.3%

Abbreviations: ABI – abiraterone; ACM – appraisal committee meeting; ADT – androgen deprivation therapy; EAG – external assessment group; ENZ – enzalutamide; mCRPC – metastatic castration resistant prostate cancer; OLA – olaparib

Time on treatment

Background: Company submitted partitioned survival model with 3 health states: rPFS, progressive disease (PD), and death. PD health state split into time on subsequent treatment and time on palliative care.

Company

- TALA+ENZ: TTD data extrapolated using unweighted trial data (TALAPRO-2)
- OLA+ABI: Assumed TTD = rPFS based on landmark estimates from PROpel trial and CADTH submission as TTD trial data not available
- ENZ: TTD data extrapolated using unweighted trial data (TALAPRO-2 versus TALA+ENZ)
- Mean TTD: [redacted] months for TALA+ENZ and [redacted] months for OLA+ABI

EAG comments: TALA+ENZ: rPFS was longer in weighted data compared with unweighted data. Similar result expected with TTD. Using unweighted TTD favours TALA+ENZ (see appendix)

- OLA+ABI: TTD assumption did not align with prior NICE and CADTH appraisals:
  - CADTH assumed lower TTD than rPFS: rPFS (TTD) at 15 years = 12% (5%), 20 years = 7% (3%)
- EAG base case (based on clinical expert) assumed relationship between TTD and rPFS observed for:
  - TALA+ENZ applied to OLA+ABI and
  - ENZ applied to ABI

At FAC EAG note→ scenario where TTD=rPFS for all treatments is a reasonable alternative but may overestimate all treatment costs

	Mean rPFS (months)	Mean TTD (months)
TALA+ ENZ	Unweighted: [redacted] Weighted: [redacted]	Unweighted: [redacted] Weighted: [redacted]
OLA+ ABI	Unweighted: [redacted] Weighted: [redacted]	Unweighted: [redacted] Weighted: [redacted]

Abbreviations: CADTH, Canada's Drug Agency; EAG – external assessment group; FAC, factual accuracy check; ENZ – enzalutamide; OLA – olaparib; PD, progressive disease rPFS: radiographic progression-free survival; TTD, Time to treatment discontinuation

Time to treatment discontinuation and rPFS comparison

TTD and PFS comparison

[redacted]

TTD KM vs curve

[redacted]

Abbreviations: ENZA – enzalutamide; KM – Kaplan-Meier; (r)PFS – (radiographic) progression free survival; TALA – talazoparib; TTD – time to treatment discontinuation

PH assumption – overall survival (TALAPRO-2)

Log-cumulative hazard plot, all-comers population

Hazard plot, all-comers population

Schoenfeld residuals plot and test, all-comers population

Company: Overall, PH assumption reasonable for OS

- Log-cumulative hazard plot: approx. parallel throughout follow-up – some overlap during start of follow-up acceptable
- Schoenfeld residuals plot: Residuals form approx. straight line, and statistical test not significant (p=0.8358)
- Hazard plot: demonstrate that the smoothed hazard over time for both treatments have a similar distributional shape

NICE

Abbreviations: OS – overall survival; PH – proportional hazard

PH assumption – rPFS (TALAPRO-2)

Log-cumulative hazard plot, all-comers population

Hazard plot, all-comers population

Schoenfeld residuals plot and test, all-comers population

Company: Overall, some concerns PH assumption holding for rPFS

- Log-cumulative hazard plot: relatively minor crossing and only early in trial period, curves then approx. parallel from ~10 months
- Schoenfeld residuals plot: p=0.0238 – some evidence against PH assumption, indicating evidence of time-varying effects
- Hazard plot: demonstrated that the smoothed hazard over time for both treatments have a similar distributional shape

Abbreviations: PH – proportional hazard; rPFS – radiographic progression-free survival

PH assumption – overall survival (COU-AA-302)

Kaplan-Meier

Log-cumulative hazard plot

Schoenfeld residuals plot and test

Smoothed hazard plot

Company: No evidence against proportional hazards assumption

Abbreviations: AAP – abiraterone and prednisolone; BSC – best supportive care; OS – overall survival; PH – proportional hazard

PH assumption – PFS (COU-AA-302)

Kaplan-Meier

Log-cumulative hazard plot

Schoenfeld residuals plot and test

Smoothed hazard plot

Company: Schoenfeld plot and test give some evidence against proportional hazards assumption

Abbreviations: AAP – abiraterone and prednisolone; BSC – best supportive care; PH – proportional hazard; PFS – progression-free survival

PH assumption – overall survival (NCT02294461)

Kaplan-Meier

Log-cumulative hazard plot

Schoenfeld residuals plot and test

Smoothed hazard plot

Company: No evidence against proportional hazards assumption

Abbreviations: BSC – best supportive care; ENZA – enzalutamide; OS – overall survival; PH – proportional hazard

PH assumption – PFS (NCT02294461)

Kaplan-Meier

Log-cumulative hazard plot

Schoenfeld residuals plot and test

Smoothed hazard plot

Company: Kaplan-Meier, log-cumulative hazard, Shoenfeld residual plot, and test, suggest proportional hazard assumption does not hold

Abbreviations: BSC – best supportive care; ENZA – enzalutamide; PH – proportional hazard; PFS – progression-free survival

PH assumption – overall survival (PROpel)

Kaplan-Meier

Log-cumulative hazard plot

Schoenfeld residuals plot and test

Smoothed hazard plot

Company: Schoenfeld test gives some evidence against proportional hazards assumption, but other diagnostics do not suggest this

Abbreviations: AAP – abiraterone and prednisolone; OLAP+AAP – olaparib with abiraterone and prednisolone; OS – overall survival; PH – proportional hazard

PH assumption – PFS (PROpel)

Kaplan-Meier

Log-cumulative hazard plot

Schoenfeld residuals plot and test

Smoothed hazard plot

Company: No evidence against proportional hazards assumption

Abbreviations: AAP – abiraterone and prednisolone; OLAP+AAP – olaparib with abiraterone and prednisolone; PH – proportional hazard; PFS – progression-free survival

Enzalutamide OS extrapolations (1/2)

Enzalutamide KM for OS overlaid with the extrapolated parametric survival curves

Abbreviations: AIC – Akaike information criterion; BIC – Bayesian information criterion; ENZA – enzalutamide; KM – Kaplan Meier; OS – overall survival

Enzalutamide OS extrapolations (2/2)

Distribution	Enzalutamide OS					
	12 months (%)	24 months (%)	36 months (%)	48 months (%)	60 months (%)	120 months (%)
KM data	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Log-logistic	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Gamma	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Generalized gamma	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Weibull	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Log-normal	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Gompertz	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Exponential	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: AIC – Akaike information criterion; BIC – Bayesian information criterion; KM – Kaplan-Meier; OS – overall survival

Enzalutamide rPFS extrapolations (1/2)

Enzalutamide KM for rPFS overlaid with the extrapolated parametric survival curves

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion; KM, Kaplan Meier; rPFS, Radiographic progression or death;

Enzalutamide rPFS extrapolations (2/2)

Distribution	Enzalutamide rPFS					
	12 months (%)	24 months (%)	36 months (%)	48 months (%)	60 months (%)	120 months (%)
KM data	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Log-normal	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Generalized gamma	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Log-logistic	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Weibull	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Gompertz	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Exponential	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Gamma	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: AIC – Akaike information criterion; BIC – Bayesian information criterion; KM, Kaplan Meier; OS, Overall survival; rPFS, Radiographic progression or death;