National Institute for Health and Care Excellence

Health Technology Evaluation

Durvalumab with platinum-based chemotherapy, then with or without olaparib, for treating newly diagnosed advanced or recurrent endometrial cancer ID6317

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	AstraZeneca	AZUK agree that it is appropriate to evaluate this technology through the single technology appraisal (STA) process.	Thank you for your comment. No action required.
	Peaches Womb Cancer Trust	An evaluation of this topic via the single technology appraisal route is appropriate.	Thank you for your comment. No action required.
Wording	AstraZeneca	The draft remit/evaluation objective only mentions durvalumab as the subject of the appraisal. AstraZeneca suggest that this should be updated to also include olaparib, e.g., “To appraise the clinical and cost effectiveness of induction durvalumab in combination with platinum-based chemotherapy, followed by maintenance durvalumab with or without olaparib within their marketing authorisations…”.	Thank you for your comment. The wording of the remit has been amended to “appraise the clinical and cost effectiveness of

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			durvalumab in combination with platinum-based chemotherapy followed by maintenance durvalumab with or without olaparib, within its marketing authorisation, for the treatment of newly diagnosed advanced or recurrent endometrial cancer."
	Peaches Womb Cancer Trust	Yes, the remit is reflective of the issues of clinical and cost effectiveness.	Thank you for your comment. The scope has been updated to reflect this.
Timing Issues	AstraZeneca	No comments.	No action required.
	Peaches Womb Cancer Trust	There is an urgent need for curative treatments for those with high risk endometrial cancer that are more widely accessible to all. More effective options for those diagnosed with a recurrence of their endometrial cancer is also required. Improved long term survival and quality of life are important to patients, and have the potential to reduce health care costs associated with treatment morbidity and palliative treatment. We would therefore argue that this evaluation is required urgently.	Thank you for your comment. NICE has scheduled this topic into its work programme. This will be appraised within its marketing authorisation. For further details, please see the NICE website:

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			https://www.nice.org.uk/guidance/indevelopment/gid-ta11340 No action required.
Additional comments on the draft remit	AstraZeneca	N/A	No action required.
	Peaches Womb Cancer Trust	No comments	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	AstraZeneca	On page 2, under the subtitle of "the technology", there is a sentence which describes the comparison which was studied in the DUO-E trial. This sentence does not fully outline the comparison considering both the induction and the maintenance settings. AZUK propose that this sentence should be updated to read: "*The trial ~~compared~~ evaluated durvalumab in combination with first line carboplatin-paclitaxel chemotherapy followed by maintenance durvalumab (with or without olaparib) compared with carboplatin-paclitaxel chemotherapy alone, followed by placebo in the maintenance setting."*	Thank you for your comment. The scope has been updated to reflect this.
	Peaches Womb Cancer Trust	The definitions and endometrial cancer statistics are correct.	Thank you for your comment. No action required.

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Population	AstraZeneca	No comments	No action required.
	Peaches Womb Cancer Trust	Yes	Thank you for your comment. No action required.
Subgroups	AstraZeneca	AZUK agree that it is appropriate and feasible to explore DUO-E subgroups according to MMR status. AZUK will endeavour to explore the other subgroups listed in the draft scope where possible, but would like to highlight the following limitations which may affect the feasibility and reliability of such analyses for decision making: **Local vs. metastatic recurrence:** In the DUO-E trial, both newly diagnosed and recurrent patients were enrolled. Within the newly diagnosed population, a subgroup analysis has been conducted to report the PFS benefit according to the FIGO stage of their disease, (which provides details on whether they had local or metastatic disease). However, within the recurrent population, no subgroup analysis has been conducted to further segment such patients into local or metastatic recurrence. The data to inform such a subgroup analysis may not be readily available. **With or without primary debulking:** Across the 3 treatments arms in the DUO-E trial, only a small proportion (13.4% to 16.2%) received no debulking surgery.(1) The reliability of such a subgroup analysis would therefore be limited by small sample sizes.	Thank you for your comment. The subgroups have been kept inclusive to allow committee to consider any subgroups it considers relevant. No action required.

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		Furthermore, the decision to offer primary debulking surgery is based on multiple clinical tumour characteristics, as well as subjective local and regional clinician preferences. This would confound the results of such an analysis and limit its value for decision-making. **PD-L1 expression** AZUK will endeavour to provide available subgroup analyses relating to PD-L1 expression, but would like to highlight that this should not be a core focus of the appraisal, for several reasons. Firstly, such a subgroup analysis was not requested in the final scope for the recent appraisal of dostarlimab in this setting [TA963], despite the fact that PD-L1 status was assessed in the RUBY trial, according to the published protocol.(2) Based on this precedent, it does not seem appropriate to focus heavily on this subgroup within the DUO-E trial either. Secondly, PD-L1 status was not a stratification factor in the DUO-E trial, and was only an exploratory analysis for PFS (i.e., the DUO-E trial was not powered for this analysis). As such, it would not be possible to guarantee that patients with PDL1+ or PDL1- disease would be well-balanced in terms of baseline characteristics or other biomarkers. Therefore, any such analysis would need to be interpreted with caution and is unlikely to be sufficiently robust for decision making. Thirdly, the clinical significance of PD-L1 expression in endometrial cancer (EC) requires further exploration and research. Clinical studies have shown inconsistent results relating to its prognostic association with survival, and this impact further varies according to whether PD-L1 is measured on tumour or	

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		immune cells. The relationship between the level of PD-L1 expression and the therapeutic impact is also not straightforward.(3) There is a possibility that any observed impact of PDL-1 status could in fact simply represent a high correlation with other biomarkers; this hypothesis has not yet been tested. For these reasons, AZUK suggest that the primary focus of the appraisal should remain on the dMMR/pMMR subgroups rather than PD-L1 expression, given that the implications of MMR status are better understood, and given that this biomarker is already measured and used to inform clinical practice in the UK for EC patients.	
	Peaches Womb Cancer Trust	Appropriate subgroups proposed, if evidence allows.	Thank you for your comment.
Comparators	AstraZeneca	AZUK agrees that the appropriate comparator for this appraisal is platinum-based chemotherapy followed by routine surveillance. The draft scope also proposes that dostarlimab is a relevant comparator in the subgroup of EC patients who have high microsatellite instability (MSI-H) or mismatch repair deficiency (dMMR), subject to "ongoing" NICE appraisal. AZUK disagree that this is an appropriate comparator given that it does not meet the criteria to be considered a relevant comparator under the current NICE methods and processes. Dostarlimab has recently undergone a NICE appraisal [TA963] for the first-line treatment of MSI-H/dMMR EC patients. The final NICE guidance for this appraisal was published on the 3rd of April 2024, and concluded that dostarlimab was recommended with managed access. The managed access agreement states that a company submission to NICE for a guidance update	Thank you for your comment. During this scope consultation, dostarlimab was recommended with managed access and is therefore not a relevant comparator due to it not being recommended for routine use at this time. The scope has been amended to remove

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		is expected in September 2024. The CDF exit appraisal for dostarlimab appears to be listed as ID6415 on the NICE website, but the appraisal has not yet begun (no scoping processes have commenced, and no scheduling information is available). Paragraph 2.2.15 in the NICE processes and methods [PMG36] states that "*technologies that NICE has recommended with managed access are not considered established practice in the NHS and are not considered suitable comparators"*. Given that dostarlimab is currently in the CDF, and that the CDF-exit appraisal has not yet commenced, AZUK disagree that it is a relevant comparator under the current NICE methods and processes. Furthermore, as the company submission for dostarlimab to exit the CDF is not expected until September 2024, it would not be anticipated to enter baseline commissioning (and thus become "established practice") until early-mid 2025, assuming that the standard NICE single technology appraisal (STA) timelines are applied. The ID6415 appraisal would therefore be expected to run less than a month ahead of the ID6317 appraisal, further demonstrating that dostarlimab would not be "established practice", even by the time of the ID6317 committee meeting, and is thus not an appropriate comparator. In summary, the only appropriate comparator for this appraisal (for both the dMMR and pMMR subgroups) is therefore platinum-based chemotherapy followed by routine surveillance.	dostarlimab from the list of comparators, and hormone therapy ((such as medroxyprogesterone acetate and megestrol) has been added to the list of comparators for consistency with other scopes in this disease area.
	Peaches Womb Cancer Trust	Appropriate comparators.	Thank you for your comment. Hormone therapy ((such as medroxyprogesterone

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			acetate and megestrol) has been added to the list of comparators for consistency with other scopes in this disease area.
Outcomes	AstraZeneca	No comments	No action required.
	Peaches Womb Cancer Trust	Yes	Thank you for your comment. No action required.
Equality	AstraZeneca	No comments	No action required.
	Peaches Womb Cancer Trust	No comments	No action required.
Other considerations	AstraZeneca	No comments	No action required.
	Peaches Womb Cancer Trust	No comments	No action required.
Questions for consultation	AstraZeneca	Consultation questions relating to the pathway of care, comparators, and subgroups have been addressed above. AZUK has no further comments on the other consultation questions at this time.	Thank you for your comment. See response in comparator and subgroups sections. No action required.

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	Peaches Womb Cancer Trust	No comments	No action required.
Additional comments on the draft scope	AstraZeneca	N/A	No action required.

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

Endometriosis UK