National Institute for Health and Care Excellence

Health Technology Evaluation

Durvalumab with etoposide and platinum-based chemotherapy for untreated extensive-stage small-cell lung cancer [ID6404]

Response to stakeholder organisation comments on the review proposal 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 UK Limited	**Appropriateness of appraising this topic through the cost-comparison process** AstraZeneca believe that durvalumab with etoposide and carboplatin/cisplatin for the treatment of patients with extensive-stage small-cell lung cancer is appropriate for a cost-comparison evaluation: Both durvalumab and atezolizumab are a type of immunotherapy called checkpoint inhibitors and are in the same therapeutic class. Treatment with immuno-therapy is the recommended standard of care for extensive-stage small-cell lung cancer and atezolizumab with etoposide and carboplatin is recommended by NICE TA638 for treating patients with untreated extensive-stage small-cell lung cancer.[3-5] As mentioned in comment 2 above, durvalumab with etoposide and carboplatin/ cisplatin will be positioned for use in the same population as TA638.[3]	Thank you for your comment. This topic will proceed as a cost-comparison.

Section	Stakeholder	Comments [sic]	Action
		The CASPIAN trial demonstrates that durvalumab significantly improved the outcomes of patients with extensive-stage small-cell lung cancer when compared to treatment of etoposide and carboplatin/ cisplatin.[1] As no trials have directly compared the efficacy of durvalumab versus atezolizumab, an indirect treatment comparison was performed by AstraZeneca to compare the efficacy of durvalumab + etoposide and carboplatin/cisplatin versus atezolizumab + etoposide and carboplatin, using data from the CASPIAN and IMpower133 trials, respectively.[1-2] Overall survival data from the CASPIAN trial was compared to an Overall survival data cut-off from IMpower133 using a frequentist Bucher approach. The results of the indirect treatment comparison reported that there were no significant differences in progression-free survival, overall survival or overall safety profile between the two treatment regimens. These data demonstrate that durvalumab + etoposide and carboplatin/cisplatin is likely to provide similar or greater health benefits at similar or lower cost than atezolizumab + etoposide and carboplatin. It is therefore appropriate to evaluate durvalumab + etoposide and carboplatin/cisplatin through a cost-comparison appraisal including atezolizumab + etoposide and carboplatin as the only comparator.	
	British Thoracic Oncology Group	BTOG welcomes this re-evaluation of durvalumab for extensive stage SCLC according to the CASPIAN trial data We agree that the cost comparison evaluation process is a reasonable route since: (i) Durvalumab has similar efficacy and toxicities to atezolizumab and it will be used the same place in the treatment pathway as atezolizumab. We confirm there have been no new treatment changes since the introduction of atezolizumab.	Thank you for your comment. This topic will proceed as a cost-comparison.

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		(ii) Durvalumab will be used to treat the same population as atezolizumab (IE PS 0-1 extensive stage small cell lung cancer, first line). (iii) Durvalumab is likely to offer similar or improved health benefits to atezolizumab. BTOG suggests that NICE evaluate the CASPIAN trial data, which led to EMA/MHRA approval (Paz Ares Lancet Oncology (2019); Paz Ares ESMO Open (2022))	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Population	AstraZeneca UK Limited	**Positioning of durvalumab with etoposide and carboplatin/ cisplatin** Atezolizumab + etoposide and carboplatin is recommended by NICE as a treatment option for untreated extensive-stage small-cell lung cancer (TA638).[3] Atezolizumab + etoposide and carboplatin is routinely commissioned by the NHS and represents established NHS practice in England for patients with extensive-stage small-cell lung cancer. The positioning of durvalumab + etoposide and carboplatin/cisplatin will be consistent with the population for which atezolizumab + etoposide and carboplatin has received a recommendation for (TA638).[3] As both durvalumab + etoposide and carboplatin/cisplatin and atezolizumab + etoposide and carboplatin are immunotherapies for patients with untreated extensive-stage small-cell lung cancer, it is anticipated that they will be used in the same place within the treatment pathway.	Thank you for your comment. No change to the scope required.

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Subgroups	AstraZeneca UK Limited	**Are there any subgroups of people in whom durvalumab in combination with platinum-based chemotherapy regimens is expected to be more clinically effective and cost effective or other groups that should be examined separately?** Durvalumab + etoposide and carboplatin/cisplatin demonstrated consistent efficacy across subgroups in the CASPIAN trial. No subgroups within the population should be examined separately.[1]	Thank you for your comment. The subgroups assessed will be based on the available evidence. No change to the scope required.
	British Thoracic Oncology Group	There are no subgroups that should be examined separately	Thank you for your comment. The subgroups assessed will be based on the available evidence. No change to the scope required.
	Roche Products Ltd.	Subgroups: assess consistency of study results in subgroups defined by demographics (e.g., age, sex, and race/ethnicity), baseline prognostic characteristics (e.g., ECOG performance status, smoking status, presence of brain metastases etc.)	Thank you for your comment. The subgroups assessed will be based on the available evidence. No change to the scope required.
Comparators	AstraZeneca UK Limited	**Atezolizumab is the only relevant comparator for durvalumab in this indication**	Thank you for your comment. The comparator in the scope has been updated to atezolizumab in

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		Atezolizumab combined with etoposide and carboplatin is the only relevant comparator for durvalumab in this indication and it is most appropriate to appraise this indication via the cost-comparison route. ***Efficacy of durvalumab versus atezolizumab*** Durvalumab with etoposide and carboplatin/cisplatin is likely to provide similar or greater health benefits at similar or lower cost than atezolizumab with etoposide and carboplatin. Both atezolizumab and durvalumab are immunotherapies and therefore have the same mechanism of action. Whilst there is no head-to-head evidence comparing the efficacy of durvalumab + etoposide and carboplatin/cisplatin and atezolizumab + etoposide and carboplatin in this indication, the results from an AstraZeneca led indirect treatment comparison of data from the CASPIAN and IMpower133 trials.[1-2] (comparing durvalumab + etoposide and carboplatin/cisplatin and atezolizumab + etoposide and carboplatin) reported that there were no significant differences in progression-free survival, overall survival or overall safety profile between the two treatment regimens. The choice of platinum-based chemotherapy differs between the trials, as patients can only receive carboplatin with etoposide in IMpower133 whereas patients are allowed to receive cisplatin or carboplatin in combination with etoposide in CASPIAN based on the investigator's choice.[1-2] To account for this difference, the indirect comparisons were conducted to pool and split the etoposide and carboplatin treatments. This resulted in similar conclusions, indicating that although choice of platinum-based chemotherapy differs, this does not have an important impact. ***Efficacy of durvalumab with etoposide and carboplatin/ cisplatin versus platinum-based combination chemotherapy***	combination with etoposide and carboplatin.

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		The efficacy of durvalumab + etoposide and carboplatin/cisplatin versus etoposide and carboplatin/cisplatin alone is not clinically similar.[1] The CAPSIAN trial demonstrates that durvalumab significantly improved the outcomes of patients with extensive-stage small-cell lung cancer when compared to treatment of etoposide and carboplatin/cisplatin.[1] • Patients in the durvalumab + etoposide and carboplatin/ cisplatin arm had a statistically significant and clinically meaningful improvement in OS compared to patients in the etoposide and carboplatin group (median OS: 12.9 months versus 10.5 months, respectively; hazard ratio: 0.75 (95% CI: 0.62, 0.91), p = 0.0032) • Patients in the durvalumab + etoposide and carboplatin/cisplatin arm had a statistically significant and clinically meaningful improvement in PFS compared to patients in the etoposide and carboplatin/cisplatin group (median PFS: 5.1 months versus 5.4 months, respectively; hazard ratio: 0.80 (95% CI: 0.67, 0.96), p = 0.0157)	
	British Thoracic Oncology Group	BTOG agrees that atezolizumab is the most relevant comparator as there is only one other licensed medicine used for this same indication (atezolizumab) and is already NICE approved. Durvalumab would fit into the existing pathway for 1st line extensive stage SCLC in the same space as atezolizumab currently occupies, thereby being another treatment option for patients to have.	Thank you for your comment. The comparator in the scope has been updated to atezolizumab in combination with etoposide and carboplatin.
	Roche Products Ltd.	Comparator: there is no evidence of non-inferiority between atezolizumab and durvalumab, although there is similarity in trial design and patient population.	Thank you for your comment. The comparator in the scope

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		There is potential bias in the CASPIAN trial in terms of safety and efficacy due to the lack of blinding. Mode of Administration: Atezolizumab also available as a subcutaneous formulation, therefore the resource use (in terms of: Administration time, hospital clinic/infusion suite capacity, and hospital pharmacy aseptic unit capacity) compared with durvalumab (which is intravenous formulation only) needs to be accounted for. Chemotherapy regimens in Studies: Patients in atezolizumab IMpower133 received etoposide + carboplatin as chemotherapy during the study, whereas in the durvalumab CASPIAN study, patients received etoposide + either cisplatin or carboplatin.	has been updated to atezolizumab in combination with etoposide and carboplatin. The panel will consider whether the mode of administration affects the cost-comparison in its deliberations.
Outcomes	AstraZeneca UK Limited	**Outcomes listed** The outcomes listed are appropriate	Thank you for your comment. No change to the scope required.
	British Thoracic Oncology Group	The outcomes listed are appropriate	Thank you for your comment. No change to the scope required.
	Roche Products Ltd.	Study Endpoints: The co-primary endpoints in the atezolizumab IMpower133 study were overall survival and investigator-assessed progression-free survival, whereas the sole primary endpoint in the durvalumab CASPIAN study was overall survival	Thank you for your comment. The panel will consider the quality of evidence in its deliberations. No change to the scope required.

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Equality	AstraZeneca UK Limited	No equality considerations have been identified at this stage	Thank you for your comment. No change to the scope required.
	British Thoracic Oncology Group	We do not think there are any proposed equality issues impacting on the proposed remit and scope	Thank you for your comment. No change to the scope required.
Other considerations	AstraZeneca UK Limited	**Health-related benefits beyond the QALY calculation** It should be noted that several benefits of durvalumab in the proposed setting cannot be fully reflected in health economic models. Such uncaptured benefits include: the impact of extending remission on patient's social life, ability to work, mental health and emotional well-being, the value of having a longer time free from treatment, and the positive impact for family members and carers.	Thank you for your comment. The panel will consider whether there are any uncaptured benefits of durvalumab in its deliberations. No change to the scope required.
	British Thoracic Oncology Group	We do not think that durvalumab will result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation	Thank you for your comment. No change to the scope required.