National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer [1504]

Response to consultee and commentator 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

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	Roche Products Ltd	Yes. [redacted]	Thank you for your comment. The remit is intended to be a broad outline of the appraisal. The technology will be appraised within its marketing authorisation. No action required.
	British Thoracic Oncology Group (BTOG)	Yes	Comment noted. No action required.
Timing Issues	Roche Products Ltd	We are in agreement with NICEs current scheduling for ID1504, which is expected to allow appraisal within the normal timelines for cancer medicines and enable access for patients at the time of the expected marketing authorisation (see Comment 4 for details).	Comment noted. No action required.

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	British Thoracic Oncology Group (BTOG)	This is a priority area. This is the first combination of treatment which has increased survival in SCLC in over 20 years. The phase 3 clinical trial (IMpower-133) which underlies this technology has been completed and published. Application for a European license is underway and, if successful, is likely to be granted in the second-half of 2019.	Comments noted. No action required.
Additional comments on the draft remit	Roche Products Ltd	No additional comments.	Noted. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	British Thoracic Oncology Group (BTOG)	Yes	Comment noted. No action required.
	Roche Products Ltd	Roche considers the definitions quoted for limited and extensive SCLC to be incorrect. Instead Roche suggests the following: ● Limited disease (LD) is described as tumour confined to one hemithorax with or without loco-regional adenopathies that could be included in a single radiation field; ● Extensive disease (ED) is described as having escaped from the previous stage parameters, including the presence of hematogenous metastasis and malignant pleural effusion. The sentence regarding the '5-year survival rate of 5%' for SCLC appears to be misquoted. The cited article states a '5-year mortality rate of 90% or more'.	Thank you for your comment. The background section has been updated.

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		The statement that “An estimated 66% of those with SCLC will receive platinum-based combination chemotherapy as a first therapy” should be specified that this is for ES-SCLC patients. Roche considers ES-SCLC patients who are ineligible to receive etoposide combination regiments as being outside of the scope of this technology appraisal.	
The technology/ intervention	British Thoracic Oncology Group (BTOG)	Yes	Comment noted. No action required.
Population	British Thoracic Oncology Group (BTOG)	Yes No specific groups needs separate consideration.	Comment noted. No action required.
	Royal College of Pathologists	The main issue for pathologists in relation to treatment with this kind of drug is the probable need for an associated diagnostic test that may decide whether the patient is eligible for treatment. Data suggest that those with greater immunostaining of the tumour PD-L1 have a better response. If this is the case and it is a companion diagnostic, pathologists will have to be training in interpretation and systems for the validation will need to be put in place as well as the cost of the test (and possible rebiopsy) take into account.	Comment noted. The scope states that ‘the appraisal should include consideration of the costs and implications of additional testing for biological markers’. Additionally, the ‘other considerations’ section of the scope has been updated to include subgroup analysis.

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		Impact on biomedical scientists workloads/staff will also need to be taken into account. RCPath would therefore need to know if a test is part of the requirement and, if so which one?	
Comparators	British Thoracic Oncology Group (BTOG)	Yes. Standard treatment in the NHS is 4-6 cycles of platinum-based chemotherapy	Comment noted. No action required.
	Roche Products Ltd	As stated above, untreated ES-SCLC patients who are not eligible to receive etoposide are considered by Roche to be outside of the scope of this appraisal. In addition, Roche understands that while this list of alternative regimens for etoposide-ineligible patients reflects the ESMO guidelines, this is not reflective of NHS clinical practice. Furthermore, Roche understands from seeking clinical opinion that only between [redacted] of untreated ES-SCLC patients are expected to be ineligible for etoposide treatment.	Comment noted. The background section of the scope aims to provide a broad overview of the disease and current guidance. If specific populations are not considered by the company and if certain treatments are not used in clinical practice, this can be explained in the submission
Outcomes	British Thoracic Oncology Group (BTOG)	Yes. Standard outcomes measures described.	Comment noted. No action required.
	Roche Products Ltd	Roche agrees that the outcomes listed are important for this appraisal. We recommend that in addition NICE consider including time to treatment discontinuation and duration of response.	Thank you for your comment, the list of outcomes is not

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			exhaustive and more can be added by the company in its evidence submission to NICE if required. No action required.
Economic analysis	British Thoracic Oncology Group (BTOG)	The median survival from the	Noted. No action required.
	Roche Products Ltd	The economic analysis will follow the NICE reference case.	Comment noted. No action required.
Equality and Diversity	British Thoracic Oncology Group (BTOG)	No concerns identified.	Noted. No action required.
	Roche Products Ltd	No equality issues have been identified.	Noted. No action required.
Other considerations	British Thoracic Oncology Group (BTOG)	None	Noted. No action required.
	Roche Products Ltd	None identified.	Noted. No action required.

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Innovation	British Thoracic Oncology Group (BTOG)	Yes. Improving outcomes in extensive-stage SCLC has proven very difficult to achieve, despite multiple approaches over the years, and prognosis remains very poor. The IMpower-133 trial has shown the first improvement in Overall Survival in over 20 years and is therefore a step-change in the management of this condition. In my opinion, the additional of Atezolizumab to Etoposide and Carboplatin is the new Standard of Care. Whereas the majority of patients with extensive stage SCLC respond to first-line platinum-based chemotherapy, relapse of disease is universal and usually swift. The majority of patients in the real-world setting are too unwell to receive 2nd line chemotherapy. Consequently, any technology that improves PFS and OS, this is likely to be associated with an improvement in QALY. Formal Quality of Life data has not yet been published. Data available to the Committee will be from the IMpower-133 trial.	Comment noted. Innovation will be considered by the appraisal committee when formulating its recommendations. The consultees and commentators will have an opportunity to provide evidence on the innovative nature of the product in their submissions. No changes to the scope required.
		Atezolizumab is an innovative treatment option, which in combination with carboplatin and etoposide offers a step change in the management of first-line, ES-SCLC patients. Atezolizumab, a PD-L1 inhibitor, restores anti-cancer immunity by preventing T-cell deactivation. Data available from the phase III study IMpower133 has demonstrated significant clinical benefit of atezolizumab in combination with carboplatin and etoposide. Based on the results of IMpower133, atezolizumab in combination with carboplatin and etoposide is the first phase III immunotherapy-based combination to demonstrate a statistically significant and clinically meaningful	Comment noted. Innovation will be considered by the appraisal committee when formulating its recommendations. The consultees and commentators will have an opportunity to provide evidence on the innovative nature of the product in their

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		improvement in OS and PFS across all patients in untreated, ES-SCLC, whilst also demonstrating a safety profile consistent with known safety risks. As such, this combination provides a potential new standard of care for patients with ES-SCLC. [redacted]	submissions. No changes to the scope required.
Questions for consultation	British Thoracic Oncology Group (BTOG)	None	Noted. No action required.
	NCRI-ACP-RCP-RCR	**Have all relevant comparators for atezolizumab been included in the scope?** Platinum based chemo is the accepted standard systemic treatment **Which treatments are considered to be established clinical practice in the NHS for extensive-stage SCLC?** Platinum based chemotherapy, radiotherapy in the form of Prophylactic cranial irradiation and consolidation thoracic radiotherapy **Are the outcomes listed appropriate?** Yes **Are there any subgroups of people in whom atezolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?**	Thank you for your comment. The background section has been updated.

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		Where do you consider atezolizumab will fit into the existing NICE pathway, lung cancer? Potential first line treatment in combination with chemotherapy **Do you consider atezolizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** Yes, has the potential to change practice and introduce a new class agents in standard treatment paradigms. **Do you consider that the use of atezolizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** **Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.** Randomised phase II/III trial data (impower 133).	
	Roche Products Ltd	***Have all relevant comparators for atezolizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for extensive-stage SCLC?*** • Roche understands that the majority of untreated, ES-SCLC patients within the NHS will be treated with a platinum-etoposide regimen, with only between [redacted] of these patients being intolerant to etoposide.	Comments noted. No action required.

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		• Of these, we understand the majority of patients will be treated with carboplatin-etoposide, as this has a more manageable safety profile than cisplatin-etoposide. **Are the outcomes listed appropriate?** • As stated above, Roche agrees that the outcomes listed are important for this appraisal. We recommend that in addition, NICE considers including time to treatment discontinuation and duration of response. **Are there any subgroups of people in whom atezolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?** • **There are no known subgroups of untreated, ES-SCLC patients for whom atezolizumab plus carboplatin and etoposide treatment is expected to be more clinically effective or cost effective. Specifically, PDL-1 testing is not relevant among ES-SCLC patients. Furthermore, there is no evidence of tumour mutation burden being predictive of response.** **Where do you consider atezolizumab will fit into the existing NICE pathway, lung cancer?** • Atezolizumab plus carboplatin and etoposide is expected to be prescribed in the NHS for untreated, ES-SCLC patients. **Do you consider atezolizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?**	

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		• Atezolizumab plus carboplatin and etoposide is a substantial step-change in current treatment approaches for untreated ES-SCLC. This is due to this regimen being the first successful trial in this indication in over 30 years. [redacted] **Do you consider that the use of atezolizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** • No comment **To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.** • No barriers to adoption are expected	

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

Not applicable.