National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Nivolumab with ipilimumab and chemotherapy for untreated metastatic non-small-cell lung cancer [ID1566]

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	Bristol Myers Squibb	Yes	Comment noted. No action required.
	British Thoracic Oncology Group	Yes, assuming the marketing authorization is granted	Comment noted. No action required.
Timing Issues	Bristol Myers Squibb	There are now several treatments available for patients with untreated metastatic NSCLC (through either baseline commissioning or CDF). Nonetheless, we believe there is still considerable unmet need for a significant proportion of patients, especially those who could benefit from an immuno-oncologic (IO) treatment option with the potential to provide long-term durable response.	Comment noted. No action required.
	British Thoracic Oncology Group	The clinical community has yet to see the data. It is being presented at the ASCO20 meeting 30th May. The urgency cannot be assessed until seeing the data, since effective options already exist. However, for it would be useful to have the regime available at the same time as marketing access.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft remit	Bristol Myers Squibb	-	N/A

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Bristol Myers Squibb	Point of clarification - please note NICE TA584 & TA557 are for non-squamous NSCLC population	Comments noted. The draft scope has been updated to reflect the comments received.
	British Thoracic Oncology Group	Broadly correct	Comment noted. No action required.
The technology/ intervention	Bristol Myers Squibb	Yes	Comment noted. No action required.
	British Thoracic Oncology Group	Broadly correct	Comment noted. No action required.
Population	Bristol Myers Squibb	Yes	Comment noted. No action required.
	British Thoracic Oncology Group	The population is “Adults with untreated metastatic NSCLC without sensitizing EGFR mutations or ALK fusions”	Comment noted. The population has been updated.

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	Bristol Myers Squibb	HCPs would not normally combine docetaxel with a platinum agent. Mentioned in both squamous and non-squamous groups. Additionally, pemetrexed maintenance is only recommended for non-squamous histology, not squamous histology too, as indicated in draft scope. TA190: Pemetrexed is recommended as an option for the maintenance treatment of people with locally advanced or metastatic non-small-cell lung cancer other than predominantly squamous cell histology TA402: Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin	The comparator section in the draft scope has been updated to reflect histology status. The company can comment on the relevance of any comparator in its submission.
	British Thoracic Oncology Group	For adults with non-squamous histology • The major comparator is not mentioned, specifically: pembrolizumab-pemetrexed-cis/carbo-platin (per TA557) • The comparator carboplatin-paclitaxel-bevacizumab-atezolizumab (per TA854) is infrequently used • Comparators without pembrolizumab monotherapy or a chemotherapy-immunotherapy combination (IE chemotherapy alone) are rarely used. Broadly carboplatin-pemetrexed-pembrolizumab (TA557) is standardly used. For adults with squamous histology: • the major comparator is not mentioned, specifically: pembrolizumab-carboplatin-paclitaxel combination (per TA600). • Additionally, pemetrexed maintenance is incorrect. It is not indicated, licensed, nor funded.	Comments noted. The comparators in TA557 and TA600 are not mentioned because they are not routinely commissioned, only for use within the Cancer Drugs Fund. No action required.

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		Comparators without pembrolizumab (IE chemotherapy alone) are rarely used, broadly pembrolizumab monotherapy or pembrolizumab-carboplatin-paclitaxel combination is standard of care	
Outcomes	Bristol Myers Squibb	Yes	Comment noted. No action required.
	British Thoracic Oncology Group	Yes	Comment noted. No action required.
Economic analysis	Bristol Myers Squibb	None.	Comment noted. No action required.
	British Thoracic Oncology Group	Appropriate. The magnitude of the survival benefit associated with ipilimumab (a component the technology) can take considerable time to be demonstrated. Hence, relatively immature trial follow-up may underestimate the true magnitude of the survival benefit.	Comment noted. No action required.
Equality and Diversity	Bristol Myers Squibb	None.	Comment noted. No action required.
	British Thoracic Oncology Group	I do not foresee any equality concerns.	Comment noted. No action required.
Other considerations	Bristol Myers Squibb	None.	Comment noted. No action required.
	British Thoracic Oncology Group	I agree that analysis by PDL1 status is the principal discriminator of benefit. However, this may not be important as the benefit of ipilimumab combinations in other diseases is not directly PDL1-related.	Comment noted. Appropriateness of subgroup analyses will be considered by the committee.

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		If the trial has analysed outcomes by tumour mutation burden, this may (or may not) be another biological discriminator of benefit/not, either alone or in combination with the PDL1 status.	
Innovation	Bristol Myers Squibb	CTLA-4 inhibitors have not previously been available to first-line NSCLC patients outside of a clinical trial setting; ipilimumab, a CTLA-4 inhibitor, therefore represents a new mechanism of action available to these patients, working synergistically with nivolumab, an anti-PD-1 therapy. This regimen, nivolumab in combination with ipilimumab, is preceded by two upfront cycles of chemotherapy; this has the potential to generate early response followed by long-term durable response translating into long-term survival (including incremental QALY benefit over existing SoC) and improved QoL. [redacted]	Comments noted. The company will have the opportunity to expand on the innovative potential of this technology in its submission and this will be considered by the appraisal committee
	British Thoracic Oncology Group	Yes, if approved, this would be the first time a CTLA-4 based regime would be approved for NSCLC. At time of writing we are yet to see the survival data, but CTLA4 inhibitors such as ipilimumab are associated with durable long term survival in other cancer types. QALY calculations are likely to identify the health-related benefits. The trial data underpinning the technology is the CheckMate 9-LA trial.	Comment noted. No action required.
Questions for consultation	Bristol Myers Squibb	Options for cost-effectiveness and cost-comparison approaches are being explored for the various comparators.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	British Thoracic Oncology Group	Comparators: stated as above Outcomes: listed above are appropriate Subgroups: as per comments above on tumour mutation burden and PDL1 status Place in pathway: first line for EGFR and ALK wild type, and unknown patients. Innovation: as above, although at time of writing the trial outcomes is not presented, so no firm comment can currently be made Equality: as above Benefits outside QALY: as above Dataset to consider: as above Barriers to adoption: if tumour mutation burden is considered as a subgroup, this is currently challenging to implement in UK genotyping practice. STA appropriateness: appropriate NICE methodology: I cannot comment on Health Economic details but cost comparison methodology is appropriate, the new technology may be superior in its clinical efficacy and similar in resource use to comparators (contingent on data to be presented), the trial primary outcome is still relevant, there is no new evidence.	Comments noted. No action required.
Additional comments on the draft scope	Bristol Myers Squibb	Please note the information presented in “Appraisals in development (including suspended appraisals) is not up-to-date with the NICE website.	Comment noted. This section has been updated .

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	British Thoracic Oncology Group	Atezolizumab monotherapy (ID1678) may be a comparator in the future or at the same time of implementation, contingent on timeframe of ID1678	Comment noted. No action required.

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

British Lung Foundation

The following consultees/commentators endorsed British Thoracic Oncology Group submission:

Royal College of Practitioners, Royal College of Radiologists, Association of Cancer Physicians and the National Cancer Research Institute