National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Nivolumab for previously treated gastric or gastro-oesophageal junction cancer ID1118

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	Bristol-Myers Squibb (BMS)	This is an appropriate topic for NICE to consider.	Comment noted. No action required.
Timing Issues	BMS	It is important for NICE to provide a recommendation for the use of nivolumab within the NHS as close to marketing authorisation as possible, given the limited effective treatment options currently available to these patients. Patients with advanced or recurrent gastric or gastro-oesophageal junction cancer which have previously been treated with two or more therapies including taxane have a very poor prognosis. In addition there is no standard care beyond second line. This results in uncertainty around the clinical pathway and patients are limited to either a clinical trial of or third line chemotherapy which are highly toxic and used outside their marketing authorization, or managed using best supportive care alone	Comment noted. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	BMS	The background information states the following: People may be treated with taxane (docetaxel or paclitaxel) monotherapy or combination therapy at second line, but beyond second line there is no evidence on the effective use taxanes or other chemotherapeutic agents	Comment noted. No action required
The technology/ intervention	BMS	Although the description in the draft scope is correct, it does not include the CheckMate-032 study or reference the ONO-4538-12 study. CheckMate-032 (NCT01928394) is a phase II ongoing single-arm study of nivolumab for the treatment of locally advanced or metastatic gastric or gastro-oesophageal junction cancer. [redacted] ONO-4538-12 (NCT02267343) is a Phase III randomised double-blind study conducted in Japan, Korea and Taiwan to evaluate the efficacy and safety of nivolumab in patients with unresectable advanced or recurrent gastric or gastro-oesophageal junction cancer refractory to or intolerant of standard therapy. [redacted] Nivolumab is a *human* monoclonal antibody	Comment noted. No action required. The technology section is only for a brief description of the technology and a mention of the key pivotal trials which supports the company's marketing authorisation. An in-depth description of all relevant clinical trials would be expected in the company's submission.
Population	BMS	It is anticipated that the patient population in which nivolumab may be more beneficial would be patients with [redacted]	Comment noted. No action required

Section	Consultee/ Commentator	Comments [sic]	Action
		[redacted]	
Comparators	BMS	We believe the most relevant comparator for this appraisal should be that of best supportive care. Currently there is no relevant NICE guidance describing appropriate therapies in this patient group. In this context, ESMO and NCCN guidelines may be the most relevant to clinical practice in the UK. These guidelines recommend second-line chemotherapy with a taxane (docetaxel or paclitaxel), irinotecan-based therapy or ramucirumab-based therapy in patients with an adequate performance score. However, there is no clear evidence for a benefit of these chemotherapies beyond second line treatment and all are associated with high toxicities which severely impact the quality of life of the patients. Further, as noted in the draft scope around half of new cases in the UK are diagnosed in patients aged 75 years and over. Therefore, given the age of diagnosis in the UK, any patients receiving treatment past second line may only be fit enough to receive best supportive care, given the toxicities associated with the drugs used in second line. It should also be noted that the studies providing the clinical effectiveness for nivolumab include heavily pre-treated patients, who have exhausted available treatment options, including [redacted]	Comment noted. The comparator section reflects current clinical practice and is kept broad to encompass the entire population that may be eligible for treatment within the marketing authorisation.

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		Thus, patients in these studies reflect the treatment pathway outlined in ESMO and NCCN, and are unlikely to receive subsequent treatment with other chemotherapeutic agents. Additionally, treatment of gastric cancer in previously treated patients is not included within the licensed indication for either docetaxel or paclitaxel. As noted within the NICE guide to the methods of technology appraisal, comparators technologies that do not have a marketing authorisation (or CE mark for medical devices) for the indication defined in the scope can be considered when they are considered to be part of established clinical practice for the indication in the NHS. However, during NICE TA378, it was noted that the vast majority of patients receive best supportive care at second line (71.5%), with 28.5% of patients receiving chemotherapy, comprised primarily of docetaxel (8.0% of second-line patients) and paclitaxel (3.0%). In addition, the submission notes that only 12% of patients receive a subsequent (third-line) chemotherapy, based on market research data. Based on this evidence, it can be concluded that 88% of patients receive best supportive care, with small proportions of patients receiving other therapies. Thus, any chemotherapy used in this setting is unlikely to comprise established clinical practice in line with NICE guidance.	
Equality and Diversity	BMS	No equality issues have been identified.	Comment noted. No action required
Innovation	BMS	BMS consider nivolumab to be innovative in the treatment of advanced gastric or gastro-oesophageal junction cancer, due to its novel mechanism of	Comment noted. No action required

Section	Consultee/ Commentator	Comments [sic]	Action
		action in this therapeutic area and the potential for it to make a significant impact on the substantial unmet need. Nivolumab is a novel immunotherapy agent for the treatment of cancer, with a new mechanism of action as a highly specific programmed death-1 (PD-1) immune checkpoint inhibitor. It specifically binds to PD-1 receptor on the surface of immune cells and restores T-cell activity by blocking the binding of the PD-L1 and PD-L2 ligands found at the tumour site to PD-1 receptors on immune cells. This approach, enabling the body's own immune system to target cancer, is novel in gastro-oesophageal cancer and is viewed by physicians and patient interest groups as a 'step-change' in its management. In patients with advanced or recurrent gastro-oesophageal cancer, outcomes are poor, with very short survival and few recommended treatment options, so that there is significant unmet need in this patient population. Based on available data relating to nivolumab, this is of major interest for public health, in particular from the view point of therapeutic innovation, as it has the potential to offer an alternative therapeutic option with an expected improved significant benefit over management of patients in the absence of nivolumab.	

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

Department of Health