National Institute for Health and Care Excellence

Single Technology Appraisal (STA/MTA)

MABp1 for treating metastatic or unresectable colorectal cancer after oxaliplatin and irinotecan

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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
Appropriateness	XBiotech	Yes	Comment noted.
Wording	XBiotech	Yes	Comment noted.
Timing Issues	XBiotech	[redacted]	Comment noted.
Additional comments on the draft remit		None	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background	XBiotech	This is accurate	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
information			
The technology/ intervention	XBiotech	Yes	Comment noted.
Population	XBiotech	The 2014-PT026 trial (EudraCT number 2014-000550-12) included only patients with symptoms associated with their malignancy. This population had an ECOG score of 1 or 2, and included patients over the age of 70. These patients may be too frail to derive as much benefit from conventional, cytotoxic or targeted therapies due to the associated toxicities. Treatment with an agent that improves symptoms as the result of an anti-neoplastic effect is thus of particular importance.	Comment noted.
Comparators	XBiotech	The comparators in both phase 3 trials are best supportive care, and do not include agents with a proven anti-neoplastic effect.	Comment noted.
Outcomes	XBiotech	The primary endpoints for The 2014-PT026 trial (EudraCT number 2014-000550-12) are measures designed to assess the reversal of cancer associated symptoms. In the setting of refractory, metastatic disease, reversal of muscle loss, appetite loss, pain, and fatigue, secondary to an antineoplastic effect, represents an important clinical benefit for patients that may otherwise be too symptomatic to continue with conventional cytotoxic regimens.	Comment noted. Reversal of cancer associated symptoms has been added to the outcomes in the scope.
Economic analysis	XBiotech	Patients with symptomatic, metastatic colorectal cancer, that is refractory to standard therapies, would be expected to have a median survival of 4-6 months.	Comment noted
Equality and Diversity	XBiotech	We do not anticipate that the proposed remit and scope will adversely exclude or have an adverse impact on any of the populations mentioned.	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
Innovation	XBiotech	A determination of median overall survival in response to therapy is an unequivocal objective response. However, these studies can be large, costly and require a considerable amount of time in which to collect survival data. Moreover, survival results do not provide any insight regarding the patient quality of life while on therapy, which can be an important consideration particularly when the improvement in overall survival is modest and the therapy is associated with considerable toxicities. Alternatively, efficacy of anti-cancer therapies may be evaluated based on "tumor responses," as measured by radiologically evident decreases in dimensions of tumor lesions. For six decades, tumor response has been used as a measure of objective response and a primary endpoint in oncology. In advanced metastatic disease, however, the use of tumor responses to assess anti-cancer therapy has fundamental challenges. Few agents have been found to reliably mediate durable tumor responses in the context of metastatic solid tumors. Typically tumor responses are both modest and transient and thus equivocal in terms of prognostic value for survival. Tumor response findings do not generally provide insight into the clinical benefit of the therapy, such as reduction in disease-related morbidity. Moreover, in an effort to cultivate agents that can achieve tumor responses, developers have focused on the advance of cytotoxic agents that carry with them significant trade-off in terms of treatment-related morbidity. New agents, such as the Xilonix antibody therapy, may be designed to mediate anti-tumor, disease modifying activity that may prolong life, reduce both treatment and disease-related morbidity, and improve life quality without a significant demonstration of cytotoxicity. For this kind of agent, using tumor responses as a primary measure of efficacy fails to provide insight into its	Comment noted. The appraisal will consider health related quality of life as well as overall survival. Response rate has been removed from the outcomes section of the scope. The potential for MABp1to be considered an innovative technology will be considered by the Appraisal Committee at the appraisal stage.

Section	Consultee/ Commentator	Comments [sic]	Action
		treatment potential. The 2014-PT026 study thus represents a necessary and groundbreaking step to establish new objective response criteria to evaluate modern cancer therapies such as the true human therapeutic antibody under study. The findings from this trial are the first evidence that an objective response criteria based on radiological assessment not of tumor mass but of lean body mass, combined with patient self-reporting of well being, can be used to evaluate an anti-tumor therapy. A reduction in the incidence of serious adverse events (in patients receiving antibody therapy compared to placebo) was both a novel finding for an oncology therapy and a corroboration of the objective response criteria. New clinical endpoints are needed to evaluate anti-cancer agents with respect to their potential to prolong and improve the life of cancer patients. The Xilonix antibody was expected to antagonize the local and distal effects of tumor pathophysiology without principally acting as a cytotoxic agent. In using an antibody with exceptional tolerability, the objective was to reduce therapy related morbidity and improve the lives and survival of persons with disseminated malignancy. These findings confirm the potential for a new antibody therapy for colorectal cancer—and opens the door to novel thinking about how cancer agents may be conceived and developed to improve the health and overall survival of patients living with cancer.	
Other considerations		None	

Section	Consultee/ Commentator	Comments [sic]	Action
Questions for consultation		None	
Additional comments on the draft scope		None	

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

Department of Health