National Institute for Health and Care Excellence

Health Technology Evaluation

Pembrolizumab with trastuzumab and chemotherapy for untreated locally advanced unresectable or metastatic HER2-positive gastric or gastro-oesophageal junction adenocarcinoma [ID3742]

Response to stakeholder organisation 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 and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	MSD	Yes, the remit is appropriate.	Thank you for your comment. No action required.
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	This is certainly a worthwhile evaluation. The initial results of the Keynote-811 study are certainly very promising but no data is yet available on benefits to survival. This evaluation is appropriate as its primary outcomes include survival and QOL,.	Thank you for your comment. No action required.
Wording	MSD	Yes, the wording is appropriate.	Thank you for your comment. No action required.

Section	Stakeholder	Comments [sic]	Action
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	Yes	Thank you for your comment. No action required.
Timing Issues	MSD	There is currently a high unmet need in this patient population, therefore scheduling an appraisal in line with the regulatory submission timelines would be appropriate.	Thank you for your comment. No action required.
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	Urgent as most GOJ cancers are incurable at diagnosis and importantly, demonstration of clinical effectiveness may lead to this drug combination being used for neo-adjuvant chemotherapy with a potential benefit for patients going down a curative route where currently cure rates are low.	Thank you for your comment. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	MSD	Background information is accurate and complete.	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	It would be useful to reference the latest trial data rather than just the NICE recommendations.	Thank you for your comment. The background information section of the scope provides a brief overview of the condition. No action required.
Population	MSD	The population is defined appropriately.	Thank you for your comment. No action required.
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	Yes	Thank you for your comment. No action required.
Subgroups	MSD	MSD does not expect subgroup data based on specific IHC score to be available. Patients with HER2-positive status, defined as either IHC 3+ or IHC 2+ in combination with ISH+ (or FISH), as assessed by central review on primary or metastatic tumour, are the main trial population. Subgroup data based on PD-L1 status is expected to be available.	Thank you for your comment. Subgroup data will only be considered if the evidence allows. This section has been amended to include PD-

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			L1 status as a subgroup to consider.
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	Potentially. PD-1/PD-L1 status should be used for subgroup analysis.	Thank you for your comment. Subgroup data will only be considered if the evidence allows. This section has been amended to include PD-L1 status as a subgroup to consider.
Comparators	MSD	NG83 clinical guidance recommends that patients with untreated HER-2 positive gastric and gastro-oesophageal junction cancer should be offered trastuzumab in combination with cisplatin and capecitabine or 5-fluorouracil. Therefore, we believe that doublet and triplet chemotherapy regimens without trastuzumab are not relevant for the appraisal of HER-2 positive untreated gastric and gastro-oesophageal cancer.	Thank you for your comment. NG83 also recommends chemotherapy regimens to people with advanced oesophago-gastric cancer. The comparators therefore remain unchanged. Stakeholders can provide justification around the most appropriate comparators and the committee will consider

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			this during the appraisal.
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	Yes	Thank you for your comment. No action required.
Outcomes	MSD	MSD considers that the outcome measures listed are appropriate.	Thank you for your comment. No action required.
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	Yes but personally I am sceptical about the use of progression free survival and response rates in this case as this is an aggressive disease where survival is short so there should be no need for what are essentially surrogate endpoints. Survival and QOL are key.	Thank you for your comment. The outcomes are kept broad at this stage. The committee will consider the most appropriate outcomes during decision making. No action required.
Questions for consultation	MSD	**Where do you consider pembrolizumab with trastuzumab and chemotherapy will fit into the existing care pathway for untreated HER2-positive advanced gastric or gastro-oesophageal junction cancer?** MSD expects that the combination of pembrolizumab with trastuzumab and chemotherapy will be used in line with its expected marketing authorisation in	Thank you for your comments. No action needed.

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		advanced metastatic settings: [redacted] **Should any other subgroups be considered e.g. people with tumours expressing PD-L1?** MSD considers pembrolizumab with trastuzumab in combination with chemotherapy to offer clinical benefit within the ITT population of patients with HER2 positive advanced gastric or gastro-oesophageal junction adenocarcinoma, as per the expected results from KEYNOTE-811 trial. **Would pembrolizumab with trastuzumab and chemotherapy be a candidate for managed access?** The submission to NICE will be made based on data from an interim analysis of KEYNOTE-811. Further follow-up date will become available in the future, which may mean it is appropriate to consider this technology as a candidate for managed access. **Do you consider that the use of pembrolizumab with trastuzumab and chemotherapy can result in any potential 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 committee to take account of these benefits.**	

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		MSD does not consider that the use of pembrolizumab with trastuzumab and chemotherapy will result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation.	
	British Association of Surgical Oncology ~ The Association for Cancer Surgery	This technology should fit seamlessly into the current existing care pathway. It probably is appropriate for consideration for managed access a s the initial results from Keynote-811 are very encouraging.	Thank you for your comment. No action required.