National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Capmatinib for treating locally advanced or metastatic non-small-cell lung cancer with METex14 skipping mutations [ID1387]

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	Novartis	It is appropriate that this topic is referred to NICE for appraisal since there remains an unmet medical need for therapies that specifically target METex14 mutated advanced lung cancer.	Comment noted. No action needed.
Wording	Novartis	The wording of the remit appropriately reflects the clinical and cost-effectiveness issues that the technology should consider.	Comment noted. No action needed.
Timing Issues	Novartis	METex14 mutated advanced lung cancer represents approximately 4% of lung cancer patients and has a particularly poor prognosis. This topic is highly appropriate and urgent given that there are currently no NICE approved therapies that specifically target METex14 mutated advanced NSCLC, and as such a substantial unmet need exists among patients with this aggressive form of lung cancer.	Comment noted. No action needed.
Additional comments on the draft remit	Novartis	[none]	No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Novartis	The background information is accurate.	Comment noted. No action needed.
	Sanofi	This section would benefit from some information on the prevalence of METx14 mutations compared to other biomarkers such as PD-L1/1's	Thank you for your comments. The background section is intended to provide a brief summary of the condition. More details will be discussed during the appraisal. No further action is needed.
The technology/ intervention	Novartis	The description of the technology is accurate.	Comment noted. No action needed.
Population	Novartis	The population is appropriately defined and in line with the population included in GEOMETRY-mono-1, the clinical trial underpinning this indication.	Comment noted. No action needed.
	Sanofi	Is the population of interest treatment naïve i.e. capmatinib for first-line treatment of METex14 skipping mutations, in patients without EGFR, ALK or ROS-1 abberations, or is it proposed that capmatinib may be used following other first-line/second-line treatment options?	Thank you for your comment. The committee will consider capmatinib in line with its marketing authorisation. The committee will consider the positioning of capmatinib during the

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			appraisal. No action needed.
Comparators	Novartis	The draft scope comprehensively describes the comparators for capmatinib according to histology, PD-L1 status and line of therapy. However, we note that: • The main comparators for capmatinib are likely to be immunotherapies and/or chemotherapy • The comparators nivolumab plus ipilimumab (ID1566) and tepotininib monotherapy (ID3761), cannot currently be considered as standards of care since they are subject to ongoing appraisals (as indicated). • Pembrolizumab with carboplatin and paclitaxel (TA600) is currently recommended within the Cancer Drugs Fund and therefore cannot be considered as a comparator The comparator atezolizumab plus bevacizumab, carboplatin and paclitaxel in patients who previously failed prior EGFR or ALK directed therapy (TA584) is not a relevant comparator for capmatinib. The METex14 skipping mutations are mutually exclusive to those with EGFR or ALK mutations (or ROS-1) and are distinct populations.	Thank you for your comment. The list of comparators within the scope is kept broad to be inclusive of all potentially relevant comparators. The company can provide explanations within its submission regarding which comparators are considered relevant or not.
	Sanofi	How will the appraisal address the uncertainty surrounding the efficacy of the intervention in patients with high PDL-1 expression. It is only this population for which PD1/L1s are relevant comparators. Will subgroup data be available? Will an analysis of METex14 and PD-L1 positive (of various levels) patients be available for both the intervention and the comparators?	Subgroup analysis based on expression of PD-L1 has been recommended in the 'other considerations' section. The committee may consider differences between subgroups as data allows during the

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			appraisal. No action needed.
Outcomes	Novartis	The outcome measures should reflect those assessed in the key trial (GEOMETRY mono-1) for the intervention being appraised. As such, all the outcomes listed in the draft scope are appropriate	Comment noted. No action needed.
Economic analysis	Novartis	The economic analysis is appropriate and consistent with the NICE reference case. With regards to the cost of diagnostic testing, it is anticipated that genomic testing for METex14 skipping mutations in NSCLC will be added to the National Genomics Test Directory imminently. It is further anticipated that the technology for delivery will be via NGS panel. The current cancer test directory already includes multi-target NGS panels for small variants (EGFR, ALK, BRAF, KRAS) and structural variants (ROS1, RET, ELM4-ALK, NTRK1-3) in NSCLC at diagnosis. As such, the costs associated with diagnostic testing for METex14 skipping mutations in advanced NSCLC will be explored in sensitivity analyses in the economic modelling.	Comment noted. No action needed.
	Sanofi	How does the appraisal plan to address the question of treatment sequencing in this population?	Thank you for your comment. Treatment sequencing may be considered by the committee during the appraisal. It is beyond the remit of the scope. No action needed.
Equality and Diversity	Novartis	No Comment	No action needed.

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Other considerations	Novartis	According to NG122, Lung cancer: diagnosis and management (2019), patients with a sensitising mutation should receive a targeted agent as first-line therapy[1]. This is supported by the NHS England National Optimal Lung Cancer Pathway (V3 2020)[2], which states molecular testing results should be available 10 days after tissue acquisition. Recent reports have identified that while >80% of NSCLC patients receive recommended biomarker testing in England, the median time from tissue acquisition to availability of results of molecular results is ~18 days[3]. Furthermore, as NGS panels, rather than single gene testing, become the standard of care for the molecular testing of advanced NSCLC this can impact of further delays in turnaround time (NHSE current guidance for reporting somatic NGS panels within 21 calendar days)[2] . Timely genomic testing is critical to ensure patients receive access to innovative treatments for their disease. As mentioned earlier, it is anticipated that genomic testing for METex14 skipping mutations will be included in the national testing directory and delivered by NGS panel. This is also in line with recent international recommendations to consider inclusion of MET where there is a broad panel approach for NSCLC diagnosis in use; National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), College of American Pathologists (CAP)/International Association for the Study of Lung Cancer (IASLC)/Association for Molecular Pathology (AMP) guidelines. It will be important that METex14 testing is fully embedded in the lung diagnostic pathway. In addition, salvage and fast-track/urgent testing pathways and consideration of liquid biopsy (where tissue sample are not	Thank you for your comment. Testing for METex14 mutations in the NHS will be considered by the committee during the appraisal. No action needed.

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		available) need to be optimised to ensure that patients are offered appropriate treatment options.	
Innovation	Novartis	Capmatinib belongs to a class of CMET inhibitors that specifically target MET alterations, including those in lung cancer, and therefore fulfils a long-recognised and urgent medical need for a treatment option to specifically target the drivers of lung cancer in patients with MET exon 14 skipping mutations. Capmatinib is an innovative therapy with the potential to make a significant and substantial impact on health-related benefits as demonstrated by its Breakthrough Therapy Designation by the FDA following the positive results of the pivotal GEOMETRY mono-1 trial.	Thank you for your comment. The level of innovation in the development of capmatinib will be considered by the committee during the appraisal. No action needed.
Questions for consultation	Novartis	**Have all relevant comparators for capmatinib been included in the scope?** Please refer to comments in the comparator section of this comment form. **Where in the treatment pathway is capmatinib expected to be used?** Capmatinib is expected to be used in line with the GEOMETRY mono-1 trial i.e. in patients with MET ex14 skipping mutations who have not been previously treated and those who have received prior therapy **How should best supportive care be defined?** As per the NICE Guidelines NG122 for Lung cancer: diagnosis and management (2019)[1], Best supportive care may be defined as palliative care, palliative radiotherapy, additional monitoring requiring additional health care resources, and symptom control.	Thank you for these comments. Please see responses to other comments within this form. No action needed.

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		Are the outcomes listed appropriate? Please refer to comments in the outcomes section of this comment form. **Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom capmatinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?** The subgroups suggested in the scope are appropriate, and naturally will be dependent on the availability of data for both the technology and comparators. **Where do you consider capmatinib will fit into the existing NICE pathway, Treating non-small-cell lung cancer?** Capmatinib should be considered as a treatment option for METex14 skipping mutations alongside the current treatments options for NSCLC in the existing NICE lung cancer pathway. **NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:** • **could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which capmatinib will be licensed;** • **could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;**	

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		• **could have any adverse impact on people with a particular disability or disabilities.** **Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.** No Comment **Do you consider capmatinib 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)?** Please refer to comments in the innovation section of this comment form. **Do you consider that the use of capmatinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** No Comment **Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.** 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.** As mentioned in the other considerations section of this comment form, genomic testing could potentially be considered as a barrier to the adoption of capmatinib. It is anticipated that genomic testing for METex14 skipping mutations will soon be included in the national testing directory, however it is well	Thank you for your comment. Testing for METex14 mutations in the NHS will be considered by the committee during the

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		recognised that in order for patients to receive timely access to innovative treatments for their disease, there must be a timely and robust testing process in place. To support the timely treatment of NSCLC patients with a targeted therapy, the NHSE National Optimal Lung Cancer Pathway considers molecular testing results should be available 10 days after tissue acquisition. The recent NLCA's 2020 spotlight report of molecular testing in England and Wales revealed only 37% of NHS trusts achieved this turnaround time, with the median time being approximately18 days[3]. NGS panel testing turn-around times are also increased compared to simple targeted tests with current NHSE guideline times for somatic mutations for NGS panel within 21 days. **NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).** **NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.** • **Would it be appropriate to use the cost comparison methodology for this topic?** Cost comparison is not appropriate for this topic • **Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?**	appraisal. No action needed.

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		Comparative effectiveness to other treatments will be assessed and presented as part of this appraisal. Capmatinib is likely to be similar in resource use to the comparators previously described in the scope • **Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?** The primary outcomes measured in the trial/ used to drive the model are still relevant.	
	Sanofi	Could current therapies impact the expression of METexon 14 mutation?	Thank you for your comment. Expression of METex14 mutations may be considered by the committee during the appraisal if considered relevant. No action needed.
Additional comments on the draft scope	Novartis	None	No action needed.

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

- Pierre Fabre
- Pfizer