National Institute for Health and Care Excellence

Health Technology Evaluation

Datopotamab deruxtecan for treating advanced non-small-cell lung cancer after platinum-based chemotherapy ID6241

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	Daiichi Sankyo	Daiichi Sankyo considers it appropriate for datopotamab deruxtecan (Dato-DXd) to be evaluated via the single technology appraisal (STA) route to facilitate the publication of timely guidance to the NHS.	Thank you for your comment
	BTOG	Appropriate as single tech apprasial	Thank you for your comment
Wording	Daiichi Sankyo	Daiichi Sankyo requests that datopotamab deruxtecan be referred to either in full or using the abbreviated form 'Dato-DXd', as opposed to 'datopotamab' alone, as the mechanism of action relies on all components of the antibody drug-conjugate technology. The monoclonal antibody component (datopotamab) selectively binds to TROP2, which is expressed on the tumour cell surface. After the tumour cell internalises Dato-DXd, the payload (deruxtecan) is released thereby exerting its antitumour effect. For completeness, Dato-DXd does not currently have an MHRA marketing authorisation in any indication, and the precise wording of its licensed	Thank you for your comment. The scope has been amended to refer to the drug in full. The remit wording is kept broad until the

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		indication relevant to this appraisal is currently not available. However, it is anticipated the license will be [redacted]. Please see Daiichi Sankyo's responses in Comment 4 for further details.	marketing authorisation is granted.
	BTOG	Yes	Thank you for your comment.
Timing issues	Daiichi Sankyo	There remains an urgent need for treatment options with improved outcomes for patients with NSCLC who have progressed on standard of care. Docetaxel (± nintedanib) is currently offered in this setting, after other treatment options (such as immunotherapy, platinum chemotherapy, or genomic alteration-targeting therapy) have been exhausted.[1] mNSCLC is a very severe condition, with limited treatment options and short anticipated survival after progression on current standard of care. Outcomes associated with docetaxel are poor and are often associated with substantial tolerability issues. In the TROPION-Lung01 trial, Dato-DXd demonstrated superiority to docetaxel in terms of progression-free survival by blinded independent central review (BICR; hazard ratio: 0.75; 95% CI: 0.62, 0.91; P=0.0040).[2] In non-squamous histology, Dato-DXd showed a clinically meaningful benefit [hazard ratio: 0.63; 95% CI: 0.51, 0.79].[3] Given the benefit in progression-free survival with Dato-DXd, the limited efficacy of existing treatment options used routinely in NHS practice, and the tolerability challenges of docetaxel-based regimens, Daiichi Sankyo consider there is an urgency of this evaluation to the NHS so that patients with mNSCLC can have access to Dato-DXd as a matter of high priority.	Thank you for your comment.

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	BTOG	Medium / urgent (limited options for this patient population with poor outcomes)	Thank you for your comment.
Additional comments on the draft remit	Daiichi Sankyo	None	N/A
	BTOG	None	N/A

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Daiichi Sankyo	Trophoblast Cell Surface Antigen 2 (TROP2) is broadly expressed on NSCLC cancer cells, and while there is some evidence to suggest it is a prognostic factor for survival outcomes, its role in clinical tumourigenesis is not yet established. Therefore, we would suggest amending the following to: 'TROP2 is a biomarker which has been estimated to be expressed on 64 to 75% of NSCLC cancer cells, and its impact on overall survival is not yet established.' Daiichi Sankyo notes that NICE Guidance 122 (see interactive treatment pathway, March 2024) does not recommend pemetrexed and platinum chemotherapy for previously untreated patients with ≥50% PD-L1 expression.[1,4] Daiichi Sankyo therefore suggests that the text be revised to state that this treatment option is only recommended for previously untreated patients with <50% PD-L1 expression.	Thank you for your comments. The background has been retained in line with the cited reference however an addition has been made to clarify that this association is not fully established. The error around use of pemetrexed and platinum chemotherapy has been corrected.
	BTOG	Incorrect: If the squamous NSCLC expresses PD-L1 on ***less than 50%*** of its tumour cells people may be offered pembrolizumab (TA531) or atezolizumab (TA705) monotherapy.	Thank you for your comment this error has been corrected.

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		Should read more than. Otherwise accurate and complete background	
Population	Daiichi Sankyo	In the section titled 'The technology', the TROPION-Lung01 clinical trial population is described as '*people with stage 3B, 3C or 4 NSCLC which has progressed after treatment with platinum chemotherapy alone or with an immunotherapy or a targeted anti-cancer treatment'*. This differs slightly from the population described in the NICE scope, namely people with advanced or metastatic NSCLC which has progressed after prior treatment with platinum chemotherapy alone or with a PD-L1 or PD-1 inhibitor or a targeted anti-cancer treatment. The latter part of this description may be interpreted to mean that people had previously been treated with chemotherapy or immunotherapy or a targeted anti-cancer treatment. The inclusion criteria for TROPION-Lung01 stipulated that patients must have received at least two types of therapy from these three categories. For patients without an oncogenic driver mutation, prior treatment must have included a platinum-based chemotherapy and immunotherapy. For patients with an oncogenic driver mutation, prior treatment must have included platinum-based chemotherapy and 1-2 lines of targeted treatment directed at the oncogenic driver mutation. Although there are slight differences in the treatment pathways in early lines for patients with oncogenic driver mutations and those without, given the anticipated licence of Dato-DXd (and based on the descriptions above), in both instances, the relevant comparator(s) are expected to be docetaxel (± nintedanib). Daiichi Sankyo proposes that the population description in the table should be aligned with the description provided in the section titled 'The technology', for consistency with the anticipated license of Dato-DXd.	Thank you for your comment. The "technology" and "population" sections have been amended to clarify that people must have had platinum based chemotherapy and an immunotherapy or targeted therapy.

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	BTOG	Yes	Thank you for your comment.
Subgroups	Daiichi Sankyo	Subgroup analyses will be included in the submission dossier where evidence allows. Of note, and as described in the background section, TROP2 is widely expressed on NSCLC cells. However, the biomarker's role as a prognostic factor on survival outcomes and role in clinical physiology is not well established. In the TROPION-Lung01 trial, presenting results by TROP2 expression is not planned as it was not defined as a pre-specified subgroup or a stratification factor. Furthermore, the anticipated marketing authorisation is not expected to specify TROP2 expression levels. Therefore, Daiichi Sankyo are of the view TROP2 expression levels should be removed from the list of subgroups.	Thank you for your comment. The listed subgroups have been kept inclusive at this stage to allow committee to consider any subgroups for which evidence is identified.
	BTOG	Correct subgroups	Thank you for your comment.
Comparators	Daiichi Sankyo	Daiichi Sankyo considers docetaxel monotherapy and docetaxel + nintedanib are the relevant comparators for Dato-DXd in NHS practice in accordance with the anticipated licensed indication and the current UK treatment pathway. All patients in the TROPION-Lung01 clinical trial had received prior PBC. All patients without an oncogenic driver mutation had previously been treated with an anti-PD-(L)1 treatment aligned with the NICE treatment pathway where docetaxel ± nintedanib is a later-line option.[4] Current NHS practice does not allow for re-treatment with immunotherapy in a metastatic setting, so this means that anti-PD-L(1) monotherapy would not be considered a comparator for the majority of patients at this line.	Thank you for your comment. The comparator section has been updated.

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	BTOG	Yes	Thank you for your comment.
	Roche	Atezolizumab in combination (TA584) is noted in the background section, but not included in the PICO table.	Thank you for your comment. The background section gives a broad overview of the condition and the various treatment options, while the PICO table specifies any treatment options which are potential comparators. Given the trial design atezolizumab in combination was not considered a potential comparator.
Outcomes	Daiichi Sankyo	None	N/A
	BTOG	Yes	Thank you for your comment.
Equality	Daiichi Sankyo	None	N/A
	BTOG	No concerns	Thank you for your comment.

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Other considerations	Daiichi Sankyo	Advanced NSCLC is a very severe condition with poor outcomes and limited treatment options after progression on current standard of care. Daiichi Sankyo anticipate that this appraisal will be eligible for the application of the severity modifier weighting. Analyses of the shortfall calculation will be presented within the submission dossier.	Thank you for your comment. The committee will consider all analyses presented at the submission stage.
	BTOG	There will be complexity in assessing subgroups of oncogenic driven cancers and treatment sequence / prior treatments. These can be diverse (including KRAS). May need to consider grouping together but that may not be reflective (eg smoker-related drivers such as KRAS and non-smoking eg EGFR)	Thank you for your comment.
Questions for consultation	Daiichi Sankyo	**Where do you consider Dato-DXd will fit into the existing care pathway for the disease?** Dato-DXd is anticipated to be used in accordance with its proposed licensed indication for treating people with advanced or metastatic [redacted] NSCLC: • after platinum-based chemotherapy and anti-PD-(L)1 therapy for people without actionable genomic alterations • after platinum-based chemotherapy and targeted therapy for people with actionable genomic alterations TROP2 • **Would you expect the effectiveness of datopotamab deruxtecan to vary by level of TROP2 expression on tumours, if so how**? No, the effectiveness of Dato-DXd is not expected to vary by level of TROP2 expression on tumours. The evaluation by level of TROP2 expression was not a pre-specified subgroup in the TROPION -Lung01	Thank you for your responses to the consultation questions, these have been used while finalising the scope.

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		trial and the anticipated marketing authorisation is not expected to be restricted by level of TROP2 expression. • **If recommended, would datopotamab deruxtecan be used to treat NSCLC with a particular level of TROP2 expression?** No, as described in the background section, the role of TROP2 in the clinical pathophysiology of NSCLC is not fully established and there is no robust dataset available to support the use of Dato-DXd by level of TROP2 expression. • **Is there a diagnostic test that is used in clinical practice to detect the level of expression of TROP2 on tumour cells?** Levels of TROP2 expression can be evaluated by immunohistochemistry, though no clinically validated test is available as a companion diagnostic. **Is TROP2 expression routinely tested for in NSCLC in NHS clinical practice? If so, please provide details**. Clinical experts consulted by Daiichi Sankyo note that TROP2 expression is not routinely tested for in NSCLC in NHS clinical practice, and this is not anticipated to be necessary to inform the decision to treat with Dato-DXd in the future. **Would you expect the effectiveness of datopotamab deruxtecan to vary depending on prior treatment/s? If so, how**? The TROPION-Lung01 trial was not designed to formally assess the efficacy of Dato-DXd according to the number and/or type(s) of prior treatment(s) and is not powered to do so. **Do you consider that outcomes or responses to subsequent treatments might be different between people who have and haven't had surgery for their NSCLC?** It is not anticipated that the efficacy of Dato-DXd will differ between patients who have and have not received surgery for their NSCLC; however,	

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		TROPION-Lung01 was not designed to formally assess the efficacy of Dato-DXd according to receipt of prior surgery. **Would the technology be a candidate for managed access?** Daiichi Sankyo anticipates that routine commissioning is appropriate for Dato-DXd based on the maturity of the data available from the TROPION-Lung01 trial. **Do you consider that the use of datopotamab deruxtecan 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. Disease-specific health-related questionnaires were included in the trial, and Daiichi Sankyo intend to summarise outcomes for the NICE Committee to take into account as part of their decision-making.	
	BTOG	**Questions appropriate for consultation**	Thank you for your comment.
Additional comments on the draft scope	Daiichi Sankyo	**Dato-DXd was awarded an Innovation Passport (IP) designation from the MHRA in January 2023.**	Thank you for your comment.
	BTOG	**Nil additional.**	N/A

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

Roy Castle Lung Cancer Foundation