National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Trastuzumab deruxtecan for treating HER2-positive advanced gastric or gastro-oesophageal junction adenocarcinoma after trastuzumab-based treatment (review of TA879) [ID6680]
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 of an evaluation and proposed evaluation route	OS support	The evaluation route is appropriate.	Thank you for your comment. No action required.
	Daiichi Sankyo UK Ltd	Daiichi Sankyo considers the National Institute for Health and Care Excellence (NICE) Single Technology Appraisal (STA) route is appropriate to deliver guidance to the National Health Service (NHS) for this topic.	Thank you for your comment. No action required.
Wording	OS support	The wording is clear and reflects the issues of clinical and cost effectiveness. I do feel there may be clinical and long term cost benefits for the younger early onset patients which will be balance with older patients.	Thank you for your comment. No action required.
	Daiichi Sankyo UK Ltd	The draft remit is aligned with the marketing authorisation for trastuzumab deruxtecan (T-DXd), i.e. as monotherapy for the treatment of adult patients with advanced human epidermal growth factor receptor 2 (HER2)-positive	Thank you for your comment. Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen (1). The company submission will be consistent with the evidence available from the pivotal DESTINY-Gastric04 trial. In UK clinical practice, this positions T-DXd for use in patients with HER2-positive patients with aGA/GEJA after completion of first-line (1L) trastuzumab-based therapy or approved trastuzumab biosimilar-containing regimen.	
Timing Issues	OS support	As a patient and patient support group lead, all evaluations are urgent, if this benefits younger patients then it is even more urgent.	Thank you for your comment. Comments noted. NICE has scheduled this topic into its work programme. No action required.
	Daiichi Sankyo UK Ltd	In the UK, following progression on 1L trastuzumab-based therapy or approved trastuzumab biosimilar-containing regimen, patients with HER2-positive aGA/GEJA are typically managed with non-targeted chemotherapy or best supportive care (BSC), offering limited survival benefit. There has been no meaningful innovation in this setting, and no targeted therapies are currently available following progression on or after 1L treatment. Associated with particularly poor clinical outcomes, aGA/GEJA are aggressive malignancies (2). Survival outcomes remain poor in advanced disease; in the UK, patients diagnosed with Stage IV disease face a one-year mortality rate of approximately 79% (3) and there are no reported 5-year	Thank you for your comment. Comments noted. NICE has scheduled this topic into its work programme. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		survival statistics, reflecting the very limited life expectancy following diagnosis (4). HER2-positive tumours represent ~5–17% of GA and ~30% of GEJAs, and are associated with a more aggressive disease course and poorer outcomes compared with non-HER2-positive tumours (5-7). The introduction of HER2-targeted therapy in the 1L setting has improved outcomes in patients with HER2-positive aGA/GEJA, with median real-world overall survival (OS) from the start of 1L therapy of 11.8 months (8). Beyond its poor prognosis, aGA/GEJA places a substantial burden on patients' quality of life (QoL). Patients frequently experience debilitating symptoms, including dysphagia, asthenia, indigestion, vomiting, weight loss, early satiety and/or iron deficiency anaemia (2, 9-14). In the 2L setting, currently available palliative chemotherapy regimens are frequently associated with additional treatment-related adverse effects, further compromising QoL (2, 14), alongside substantial healthcare resource utilisation and economic burden (2, 15, 16). The lack of targeted treatment options beyond 1L, and the significant QoL burden driven by disease-related symptoms and treatment-associated toxicity, highlights a substantial and ongoing unmet need for effective HER2-targeted therapies for patients whose disease progresses following trastuzumab or trastuzumab biosimilar-containing regimen (17-19). Therefore, the evaluation of T-DXd in this setting is appropriate and urgent.	

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft remit	OS support	NA	Thank you for your comment. No action required.
	Daiichi Sankyo UK Ltd	Daiichi Sankyo notes that the listed NICE clinical guideline 83 recommendations provided in the draft remit are for 1L palliative chemotherapy for locally advanced or metastatic oesophago-gastric cancer. This should be made explicit in the draft scope. While CG83 states that 2L+ palliative chemotherapy may be considered for people with oesophago-gastric cancer, it does not recommend or specify particular treatment regimens in this setting. In addition, the other technology appraisals listed in the background, TA208 and TA191, as well as TA983 listed alongside them in the related NICE recommendations, are limited to recommendations for 1L treatment only. Consequently, the current remit focuses exclusively on 1L therapy and does not clearly outline the existing treatment pathway beyond 1L. Clarification of this within the scope would improve transparency regarding the current standard of care in later lines of treatment.	Thank you for your comment. The scope has been updated to included second line plus palliative chemotherapy may be considered for people with oesophago-gastric cancer.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	OS support	Background information is accurate and covers all known figures, the playing field is changing as I am seeing more women and early onset cancer patients coming to the support groups but the data is not there yet.	Thank you for your comment. No action required
	Daiichi Sankyo UK Ltd	This technology appraisal is specifically focused on HER2-positive advanced gastric or gastro-oesophageal junction adenocarcinoma, i.e. GA/GEJA. Daiichi Sankyo therefore considers that the terminology used in the disease background section of the draft scope is factually inaccurate. In particular, it should be explicitly stated that gastric cancer is commonly referred to as stomach cancer. Gastric cancer arises from the lining of the stomach and is biologically and clinically distinct from oesophageal cancer, which originates in the oesophagus. Although these malignancies occur in close anatomical proximity, they represent separate disease entities (5, 20). Cancers of the GEJ develop at the anatomical junction between the stomach and the oesophagus and share overlapping characteristics with both gastric and oesophageal cancers. Importantly, adenocarcinoma is the predominant histological subtype in both gastric and GEJ cancers, accounting for approximately 95% of cases (21-23). The most common forms of gastric cancer are therefore gastric adenocarcinoma and gastroesophageal junction adenocarcinoma. Clear and consistent use of this terminology would improve the accuracy and readability of the disease background section. Daiichi Sankyo recommends that this section be revised to ensure the terminology is accurate and presented in a manner that enhances overall clarity.	Thank you for your comment. The scope has been updated with some of the suggested comments. The aim of the background is to provide a very brief summary of the disease area. Further details can be included in all submissions for this evaluation for consideration by the evaluation committee.

Section	Consultee/ Commentator	Comments [sic]	Action
Population	OS support	Population is accurate but again early onset cancer is increasing.	Thank you for your comment. No action required.
	Daiichi Sankyo UK Ltd	While Daiichi Sankyo agrees that the population is appropriately defined, the submission will focus specifically on patients with HER2-positive aGA/GEJA who have experienced disease progression on or after treatment with one prior trastuzumab-based regimen. This population aligns with the available clinical evidence base, including the pivotal DESTINY-Gastric04 trial, which informs the cost-effectiveness evaluation. In the UK, it is expected that T-DXd would be used in patients with HER2-positive aGA/GEJA who have progressed on or after completion of trastuzumab-based therapy (or approved trastuzumab biosimilar-containing regimen), which is currently recommended in the 1L setting for HER2-positive aGA/GEJA (24, 25). Many patients experience rapid disease progression and clinical decline on currently available 2L treatments. As a result, relatively few patients would remain eligible for later line therapy (i.e. beyond the 2L setting), either due to declining performance status and fitness or limited survival. This further supports a focus on the population who are HER2-positive aGA/GEJA who have experienced disease progression on or after treatment with one prior trastuzumab-based regimen or an approved trastuzumab biosimilar-containing regimen, as this is the setting where patients are most likely to derive meaningful benefit from HER2-targeted treatment. This positioning reflects expected NHS clinical practice.	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Subgroups	OS support	Not considered differently but there will be differences of responses between younger and fitter patients than the known older patient.	Thank you for your comment. No action required.
	Daiichi Sankyo UK Ltd	It is well recognised that geography plays a critical role in shaping the presentation and outcomes of GA/GEJA, with pronounced differences between Western populations and East Asian populations (26-33). As such, data from Western populations with aGA/GEJA are generally considered more relevant for informing UK practice, as previously recognised during the NICE appraisals for TA208 (trastuzumab for the treatment of HER2-positive metastatic gastric cancer (25)), TA378 (ramucirumab for treating advanced gastric cancer or gastroesophageal junction adenocarcinoma previously treated with chemotherapy (34)), TA852 (trifluridine–tipiracil for treating metastatic gastric cancer or gastro-oesophageal junction adenocarcinoma after 2 or more treatments (35)) and TA983 (pembrolizumab with trastuzumab and chemotherapy for untreated locally advanced unresectable or metastatic HER2-positive gastric or gastro-oesophageal junction adenocarcinoma (24)). Therefore, the Western European population, a pre-specified strata in the pivotal trial DESTINY-Gastric04, is considered the cohort of interest for this appraisal. Further subgroup analyses are therefore not considered appropriate, as the population of interest already represents a reduced subset of the full analysis set. Moreover, all patients in the pivotal trial, DESTINY-Gastric04, had received exactly one prior line of therapy; therefore, subgroup analyses by line of therapy would not be feasible.	Thank you for your comment. Comment noted. The subgroups are kept inclusive at this stage to allow the committee the appropriateness of assessing subgroup results.
Comparators	OS support	Comparators are considered to the standard treatments available.	Thank you for your comment. Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Daiichi Sankyo UK Ltd	Palliative chemotherapy is considered the relevant comparator, reflecting active treatment in UK clinical practice for patients eligible for systemic therapy in this setting. Among the palliative regimens, taxane-based chemotherapy represents the predominant option used in routine care. Non-active management with best supportive care (BSC) is not considered a relevant comparator for patients with HER2-positive aGA/GEJA, as, where palliative chemotherapy is not considered an appropriate treatment option, T-DXd would likewise not be appropriate and would fall outside the decision problem. BSC is more commonly used when active treatment options have been exhausted or active systemic treatment is no longer suitable. Trifluridine–tipiracil is also not considered a relevant comparator as it is recommended for use after two or more treatments and therefore does not reflect current UK clinical practice in the population under consideration (i.e. patients with HER2-positive aGA/GEJA who have experienced disease progression on or after treatment with one prior trastuzumab-based regimen).	Thank you for your comment. Comment noted. The comparators list has been kept inclusive at this stage to allow all potential comparators to be considered by the committee.
Outcomes	OS support	Outcomes listed are appropriate and the order of preference for patients can vary. Well-being, mental and physical can be affected by adverse side effects of treatment and is different to health-related quality of life	Thank you for your comment. No action required.
	Daiichi Sankyo UK Ltd	Daiichi Sankyo considers the outcome measures listed in the draft scope to be appropriate as these are well recognised and accepted endpoints within oncology trials and comprise the important outcomes for the assessment of health-related benefits and harms.	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		The primary endpoint for the pivotal trial, DESTINY-Gastric04, was overall survival (36). Secondary and additional outcomes included: • Progression-free survival (by investigator [INV]) • Confirmed objective response rate (INV) • Disease control rate (INV) • Duration of response (INV) • Patient reported outcomes (EQ-5D-5L, Functional Assessment of Cancer Therapy – Gastric [FACT-Ga]) • Safety	
Equality	OS support	This will not exclude anyone. The treatment may have a different impact on older patients with other conditions than on early onset patients.	Thank you for your comment. These factors have been noted in the Equalities Impact Assessment form and will be considered by the committee during the evaluation.
	Daiichi Sankyo UK Ltd	Daiichi Sankyo is not aware of any issues of inequality in the management of aGA/GEJA in England and Wales.	Thank you for your comment. No action required.
Other considerations	OS support	NA	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Daiichi Sankyo UK Ltd	None	Thank you for your comment. No action required.

Questions for consultation	OS support	I am seeing more early onset cancers diagnosed at later stages, is this something others are seeing and will it change the age primary care see as at risk from this cancer?	Thank you for your comment. Comments noted. No action required

Section	Consultee/ Commentator	Comments [sic]	Action
	Daiichi Sankyo UK Ltd	**Where do you consider trastuzumab deruxtecan will fit into the existing care pathway HER2-positive advanced gastric or gastro-oesophageal junction cancer?** Daiichi Sankyo considers T-DXd will be positioned within the existing care pathway for patients with HER2-positive aGA/GEJA who have experienced disease progression on or after treatment with one prior trastuzumab-based regimen or approved trastuzumab biosimilar-containing regimen. **Have all relevant comparators been included in the draft scope?** Please refer to the 'Comparators' row above. **What treatment regimens might palliative chemotherapy include?** Real-world evidence published by Starling et al, 2025, derived from the Cancer Analysis System English Cancer Outcomes and Services Dataset, evaluated patients with advanced/metastatic gastric cancer or gastroesophageal junction adenocarcinoma who initiated 1L palliative treatment with a trastuzumab-based regimen between January 2015 and December 2019. This study found that in routine clinical practice, subsequent palliative chemotherapy in this population predominantly comprised taxane-based regimens, including paclitaxel and docetaxel, which together accounted for more than 67% of treatments used, alongside FOLFIRI (6.0%) and irinotecan (2.5%) (8). Furthermore, Daiichi Sankyo note that the NICE committee for TA378 (Ramucirumab for treating metastatic gastric cancer or gastro-oesophageal junction adenocarcinoma after chemotherapy), considered taxanes to be the most relevant comparator (34).	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Could you estimate what proportions of people whose cancer has progressed after prior trastuzumab treatment would have the various listed comparators (or any other comparators not listed)? Based on the real-world evidence published by Starling et al, 2025, approximately 33.3% of patients who receive trastuzumab-based 1L treatment subsequently went on to receive palliative chemotherapy in the 2L setting (8). **Which ICD codes would most accurately capture the population for this appraisal (please give ICD-O-3 codes if this would help better reflect the specific population)?** The population for this appraisal is defined using a clinical description rather than specific ICD codes. The decision problem relates to adults with advanced gastric or gastro-oesophageal junction adenocarcinoma (i.e. aGA/GEJA) who have experienced disease progression on or after treatment with one prior trastuzumab-based regimen or approved trastuzumab biosimilar-containing regimen, consistent with UK clinical practice and the population enrolled in the supporting clinical trials. **Do you consider that any real-world evidence (for example SACT data) could help inform this appraisal? If yes, please give details.** Daiichi Sankyo considers DESTINY-Gastric04 to be the most relevant data for evaluating T-DXd in this appraisal. However, real-world evidence published by Starling et al, 2025 derived from the Cancer Analysis System English Cancer Outcomes and Services Dataset, is also informative and considered supportive evidence for this appraisal (8). Since DESTINY-Gastric04 is a head-to-head comparison with ramucirumab plus paclitaxel (RAM+PTX), a regimen not reimbursed in the UK (34), the Starling et al, 2025 study provides valuable	

Section	Consultee/ Commentator	Comments [sic]	Action
		natural history evidence reflecting real-world treatment patterns and clinical practice in England. **Please select from the following, will trastuzumab deruxtecan be:** • **A. Prescribed in primary care with routine follow-up in primary care** • **B. Prescribed in secondary care with routine follow-up in primary care** • **C. Prescribed in secondary care with routine follow-up in secondary care** • **D. Other (please give details):** T-DXd will be prescribed as per option C. **For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** The comparators and subsequent treatments are delivered within a secondary care setting, with ongoing monitoring and routine follow-up conducted in secondary care. Treatment in the 2L+ aGA/GEJA setting is delivered with palliative intent to patients who remain eligible for systemic therapy, with regular hospital attendance for intravenous administration, pre-cycle clinical review and laboratory monitoring, and radiological assessment to evaluate disease progression. In all cases, treatment is continued until radiographic or clinical progression, unacceptable toxicity, or patient choice, after which patients typically receive BSC, often with palliative care involvement. Despite differences in dosing frequency and toxicity profiles, palliative chemotherapies	

Section	Consultee/ Commentator	Comments [sic]	Action
		occupy a similar position in the patient pathway and involve comparable follow-up intensity and decision-making processes within NHS clinical practice. Compared with some of the palliative chemotherapies used in the 2L+ setting, T-DXd has a less frequent dosing schedule and a standardised follow up pathway. T-DXd is administered once every 3 weeks as a single-agent intravenous infusion, rather than weekly or bi-weekly regimens, and does not require continuous infusions, ambulatory pumps, or central venous access for prolonged drug delivery. Routine precycle blood tests and clinical review are required (37-39). Trifluridine-tipiracil is indicated for metastatic gastric cancer or GEJA in adults after two or more treatments, independent of biomarker status, and is prescribed in the secondary care setting. **Would trastuzumab deruxtecan be a candidate for managed access?** Not applicable. The evidence from the pivotal trial, DESTINY-Gastric04, is considered sufficiently mature to inform decision-making. **Do you consider that the use of trastuzumab deruxtecan can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Daiichi Sankyo considers that treatment with T-DXd may result in substantial health-related benefits that are not fully captured within the QALY calculation. As aGA/GEJA is a rare and aggressive condition with very poor survival outcomes, incremental gains in survival may therefore have a heightened value that is difficult to reflect using standard utility measures. Additionally, the EQ-5D is not designed to capture gastric cancer-specific symptoms such as reflux,	

Section	Consultee/ Commentator	Comments [sic]	Action
		difficulty swallowing, dry mouth, eating and dietary restrictions, taste, abdominal pain and fullness, and dumping syndrome, which are captured in disease specific measures (40-43). Gastric cancer imposes a substantial burden on informal caregivers, particularly in relation to the intensive management of patients' nutritional needs. Caregivers commonly experience ongoing psychological distress, including reopening fear of disease progression or recurrence, and, in some cases, bereavement (44). These impacts are unlikely to be reflected in the economic model, as there is limited evidence regarding caregiver burden in this disease area. Moreover, the relationship between extended survival and caregiver burden is complex and there is no consensus on the best approach to modelling caregiver utility when there are survival gains with treatment. While DESTINY-Gastric04 includes some QoL outcomes, including the disease specific Functional Assessment of Cancer Therapy-Gastric (FACT-Ga) questionnaire, the absence of a comparator of UK clinical relevance limits the ability to fully quantify relative QoL benefits. As a result, the overall health-related benefits of T-DXd may be underestimated in the economic evaluation. **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** Sowell et al, 2025 conducted a targeted literature review (TLR) and qualitative patient interviews to identify disease and treatment-related concepts that are most important to patients with advanced gastric cancer or gastro-oesophageal junction cancer and their health-related quality of life (HRQoL) (45). Primary qualitative studies published between 2018–2021 were identified and supplemented with two earlier studies from 2017 to inform the development of	

Section	Consultee/ Commentator	Comments [sic]	Action
		a preliminary conceptual disease model and interview guide. Subsequent one-to-one concept-elicitation interviews explored symptoms, daily life impacts, experiences of care, treatment expectations and views on clinical trials. Twelve symptoms were identified as most important, each reported by at least 50% of patients with high disturbance ratings (≥5/10), including nausea, fatigue, weakness, gastrointestinal symptoms, swallowing difficulties, pain and taste alterations. In addition, 31 impacts on QoL were identified, most commonly emotional distress, limitations in daily activities, family and social disruption, and reliance on caregiver support. Overall, patients reported positive experiences of care and expressed a willingness to participate in clinical trials, with a strong preference for innovative treatments associated with fewer side effects, highlighting the central role of symptom burden and functional impact in HRQoL. Complementing these findings, Naher et al, 2023 conducted a systematic review assessing the prognostic value of patient-reported outcomes (PRO) in advanced gastro-oesophageal cancer (46). Seven studies comprising PRO data from 2,761 patients were included (two of which are UK based), with median survival ranging from 4.5–9.5 months. Across tumour subtypes, multiple QoL domains were consistently associated with overall survival. In univariable and multivariable analyses, physical functioning emerged as the most robust predictor of survival, alongside role and social functioning, pain, appetite loss/anorexia and global QoL. Emotional functioning, fatigue and limitations in mobility and self-care were also associated with survival in some studies. These findings demonstrate that HRQoL outcomes in advanced gastric/GEJ cancer are clinically meaningful to patients and important when evaluating treatment benefits in this population.	

Section	Consultee/ Commentator	Comments [sic]	Action
		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 trastuzumab deruxtecan 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** • **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.** Not applicable.	
Additional comments on the draft scope	OS support	NA	Thank you for your comment. No action required.
	Daiichi Sankyo UK Ltd	Not applicable	Thank you for your comment. No action required.

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

Servier Laboratories ltd