

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Tucatinib with trastuzumab for previously treated HER2-positive colorectal cancer

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of tucatinib with trastuzumab within its anticipated marketing authorisation for treating previously treated HER2-positive colorectal cancer.

Background

Colorectal cancer is a malignant tumour arising from the lining of the large intestine (colon and rectum). Metastatic colorectal cancer refers to disease that has spread beyond the large intestine and nearby lymph nodes. This type of cancer often first spreads to the liver, but metastases may also occur in other parts of the body, including the lungs, brain and bones. Most colorectal cancers are adenocarcinomas, these start in glands that line the insides of the colon and rectum.

There are around 42,900 new cases of colorectal cancer each year in the UK, accounting for 11% of all cancers.¹ Around 4 in 10 (43%) new cases of colorectal cancer in the UK were in people aged over 75 years, but it can affect young people too².

Human epidermal growth factor receptor 2 (HER2) is a receptor for a growth factor which occurs naturally in the body. When human epidermal growth factor attaches itself to HER2 receptors on breast cancer cells, it can stimulate the cells to divide and grow. Around 3 to 5% of metastatic colorectal cancer have HER2-positive mutations.³ There are currently no NICE recommended treatments for patients with HER2-positive metastatic colorectal cancer.

Metastatic colorectal cancer treatment aims to prolong survival and improve quality of life. Treatment can involve a combination of surgery (to resect the primary tumour or the metastases), chemotherapy (to make the tumour or metastases resectable, or to manage the cancer), biological therapy, and radiotherapy. For people with untreated metastatic colorectal cancer, [NICE technology appraisal 61](#) recommends intravenous fluorouracil/folinic acid (5-FU/FA) or capecitabine. [NICE guideline 151](#) recommends either folinic acid plus fluorouracil plus oxaliplatin (FOLFOX) or capecitabine plus oxaliplatin (CAPOX) for untreated disease. [NICE technology appraisal 709](#) recommends pembrolizumab for people with high microsatellite instability or mismatch repair deficiency.

For people with previously treated metastatic colorectal cancer [NICE guideline 151](#) recommends folinic acid plus fluorouracil plus irinotecan (FOLFIRI), after either FOLFOX or CAPOX. Established clinical management for previously treated metastatic colorectal cancer is considered to be single-agent irinotecan (after FOLFOX) or raltitrexed (for patients with advanced colorectal cancer who are intolerant to 5-FU/FA, or for whom these drugs are not suitable). [NICE technology appraisal 405](#) recommends trifluridine–tipiracil, if fluoropyrimidine-, oxaliplatin- or

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irinotecan-based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents and anti-EGFR agents have failed or when these therapies are not suitable. If standard therapies are unsuccessful, not tolerated or contraindicated, people are treated with best supportive care to manage the symptoms and complications of the condition.

Nivolumab with ipilimumab can be offered as a treatment for those with high microsatellite instability or mismatch repair deficiency after fluoropyrimidine-based combination chemotherapy ([NICE TA716](#)). For those with BRAF V600E mutation-positive metastatic colorectal cancer who have had previous systemic treatment, encorafenib plus cetuximab is a treatment option ([NICE TA668](#)).

The technology

Tucatinib (Tukysa, Seagen) with trastuzumab does not currently have a marketing authorisation in the UK for the treatment of adults with previously treated HER2-positive colorectal cancer. It is being studied in a randomized phase III study in combination with a FOLFOX regimen compared to a FOLFOX regimen alone or in combination with bevacizumab or cetuximab in people with HER2-positive metastatic and/or unresectable colorectal cancer that has not been treated in the metastatic stage.

Tucatinib has also been studied as a monotherapy and in combination with trastuzumab and/or other chemotherapy drugs in phase II trials in adults with HER2-positive metastatic colorectal cancer who have received prior treatment and have either become intolerant to the treatment or whose disease has progressed.

Intervention(s)	Tucatinib with trastuzumab
Population(s)	Adults with previously treated HER2-positive colorectal cancer
Comparators	<ul style="list-style-type: none"> • Single-agent irinotecan (after FOLFOX) • FOLFIRI (after either FOLFOX or CAPOX) • FOLFOX (after either FOLFIRI or CAPOX) • Raltitrexed (if 5-FU/FA are not suitable) • Trifluridine–tipiracil • Regorafenib • Best supportive care
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
<p>Other considerations</p>	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<p>Related NICE recommendations</p>	<p>Related Technology Appraisals:</p> <p>‘Nivolumab with ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency’ (2021). NICE Technology Appraisal 716. Review 2024.</p> <p>‘Regorafenib for previously treated metastatic colorectal cancer’ (2023). NICE technology appraisal 866.</p> <p>‘Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency’ (2021). NICE Technology Appraisal 709. Review 2024.</p> <p>‘Encorafenib plus cetuximab for previously treated BRAF V600E mutation-positive metastatic colorectal cancer’ (2021). NICE Technology Appraisal 668. Review 2023.</p> <p>‘Cetuximab and panitumumab for previously untreated metastatic colorectal cancer’ (2017). NICE Technology Appraisal 439. No current plans to review this guidance.</p> <p>‘Trifluridine–tipiracil for previously treated metastatic colorectal cancer’ (2016). NICE Technology Appraisal 405.</p> <p>No current plans to review this guidance.’</p> <p>‘Aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy’ (2014). NICE Technology Appraisal 307. Reviewed: Decision to move to static list.</p> <p>‘Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy: Cetuximab (monotherapy or combination chemotherapy),</p>

	<p>bevacizumab (in combination with non-oxaliplatin chemotherapy) and panitumumab (monotherapy) for the treatment of metastatic colorectal cancer after first-line chemotherapy' (2012). NICE Technology Appraisal 242. Reviewed: Decision to move to static list.</p> <p>Laparoscopic surgery for colorectal cancer' (2006). NICE Technology Appraisal 105. Reviewed: Decision to move to static list.</p> <p>Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer' (2003). NICE Technology Appraisal 61. Reviewed: Decision to move to static list.</p> <p>Related appraisals in development (including suspended appraisals):</p> <p>Pembrolizumab with lenvatinib for previously treated metastatic colorectal cancer'. NICE technology appraisals guidance (ID5112). Appraisal suspended.</p> <p>Nivolumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency'. NICE technology appraisals guidance (ID1136). Appraisal suspended.</p> <p>Related Guidelines:</p> <p>Colorectal cancer' (2021). NICE guideline 151. No current plans to review this guideline.</p> <p>ColonFlag for identifying people at risk of colorectal cancer' (2018). Medtech innovation briefing 142.</p> <p>Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care' (2017). Diagnostics guidance 30.</p> <p>Virtual chromoendoscopy to assess colorectal polyps during colonoscopy' (2017). Diagnostics guidance 28.</p> <p>Colorectal cancer prevention: colonoscopic surveillance in adults with ulcerative colitis, Crohn's disease or adenomas' (2011). Clinical guideline 118.</p> <p>Related Interventional Procedures:</p> <p>Selective internal radiation therapy for unresectable colorectal metastases in the liver' (2020). NICE interventional procedures guidance 672.</p> <p>Radiofrequency ablation for colorectal liver metastases' (2009). NICE interventional procedures guidance 327</p> <p>Related Quality Standards:</p> <p>Colorectal cancer' (2022). NICE quality standard 20.</p> <p>Suspected Cancer' (2017) NICE Quality Standard 124</p>
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan

	<p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 to 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>
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Questions for consultation

Where do you consider tucatinib with trastuzumab will fit into the existing care pathway for unresectable or metastatic HER2-positive colorectal cancer?

When would best supportive care be used in the treatment of unresectable or metastatic HER2-positive colorectal cancer?

Are there any subgroups for which tucatinib with trastuzumab would be expected to be more clinically and cost effective?

Do you consider tucatinib with trastuzumab to be appropriate for people with RAS wild-type and BRAF 600 metastatic colorectal cancer?

Which treatments do you consider to be the comparators of tucatinib with trastuzumab?

Would tucatinib with trastuzumab be a candidate for managed access?

Do you consider that the use of tucatinib with trastuzumab 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.

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 tucatinib with trastuzumab 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.

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NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

References

1. United Kingdom Fact sheet, [International Agency for Research on Cancer](#). Accessed May 2023.
2. Cancer Research UK, [Bowel cancer statistics](#). Accessed May 2023.
3. The Royal Marsden NHS Foundation Trust, [Colorectal cancer](#). Accessed May 2023.