NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Trifluridine–tipiracil with bevacizumab for treating metastatic colorectal cancer after 2 systemic treatments

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of trifluridine–tipiracil with bevacizumab within its marketing authorisation for treating metastatic colorectal cancer after 2 systemic treatments.

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 too[2].

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, and NICE technology appraisal 866 recommends regorafenib, if fluoropyrimidine-, oxaliplatin- or 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

Trifluridine–tipiracil (Lonsurf, Servier Laboratories) with bevacizumab does not currently have a marketing authorisation in the UK for the treatment of adults with metastatic colorectal cancer after 2 systemic treatments. It is being studied in a clinical trial (NCT04737187) compared with trifluridine–tipiracil monotherapy in adults with refractory, metastatic colorectal cancer.

Trifluridine–tipiracil monotherapy has a marketing authorisation in the UK for the treatment of adults with metastatic colorectal cancer, who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents. It is also indicated as monotherapy for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with at least two prior systemic treatment regimens for advanced disease.

Intervention(s)	Trifluridine–tipiracil with bevacizumab
Population(s)	Adults with metastatic colorectal cancer after 2 systemic treatments
Comparators	• 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 monotherapy • Regorafenib • Nivolumab with ipilimumab (where high microsatellite instability or mismatch repair deficiency is present) • Encorafenib with cetuximab • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	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.

Related NICE recommendations	**Related Technology Appraisals:** 'Nivolumab with ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency' (2021). NICE Technology Appraisal 716. 'Regorafenib for previously treated metastatic colorectal cancer' (2023). NICE technology appraisal 866. 'Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency' (2021). NICE Technology Appraisal 709. 'Encorafenib plus cetuximab for previously treated BRAF V600E mutation-positive metastatic colorectal cancer' (2021). NICE Technology Appraisal 668. 'Cetuximab and panitumumab for previously untreated metastatic colorectal cancer' (2017). NICE Technology Appraisal 439. 'Trifluridine–tipiracil for previously treated metastatic colorectal cancer' (2016). NICE Technology Appraisal 405. 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. 'Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy: Cetuximab (monotherapy or combination chemotherapy), 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. 'Laparoscopic surgery for colorectal cancer' (2006). NICE Technology Appraisal 105. 'Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer' (2003). NICE Technology Appraisal 61. **Related appraisals in development (including suspended appraisals):** 'Tucatinib with trastuzumab for previously treated HER2-positive colorectal cancer'. NICE technology appraisals guidance (ID6227). In development. 'Pembrolizumab with lenvatinib for previously treated metastatic colorectal cancer'. NICE technology appraisals guidance (ID5112). Appraisal suspended. 'Nivolumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair

	deficiency'. NICE technology appraisals guidance (ID1136). Appraisal suspended. **Related Guidelines:** 'Colorectal cancer' (2021). NICE guideline 151. 'ColonFlag for identifying people at risk of colorectal cancer' (2018). Medtech innovation briefing 142. 'Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care' (2017). Diagnostics guidance 30. 'Virtual chromoendoscopy to assess colorectal polyps during colonoscopy' (2017). Diagnostics guidance 28. 'Colorectal cancer prevention: colonoscopic surveillance in adults with ulcerative colitis, Crohn's disease or adenomas' (2011). Clinical guideline 118. **Related Interventional Procedures:** 'Selective internal radiation therapy for unresectable colorectal metastases in the liver' (2020). NICE interventional procedures guidance 672. 'Radiofrequency ablation for colorectal liver metastases' (2009). NICE interventional procedures guidance 327 **Related Quality Standards:** 'Colorectal cancer' (2022). NICE quality standard 20. 'Suspected Cancer' (2017) NICE Quality Standard 124
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019)

Questions for consultation

Where do you consider trifluridine–tipiracil with bevacizumab will fit into the existing care pathway for metastatic colorectal cancer?

Which treatments do you consider to be the comparators of trifluridine-tipiracil with bevacizumab?

When would best supportive care be used in the treatment of metastatic colorectal cancer?

Would chemotherapies be used at this point in the treatment pathway for metastatic colorectal cancer?

Would nivolumab with ipilimumab be used at this point in the treatment pathway for metastatic colorectal cancer?

Would trifluridine–tipiracil with bevacizumab be a candidate for managed access?

Do you consider that the use of trifluridine–tipiracil with bevacizumab 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 trifluridine–tipiracil with bevacizumab 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.

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 July 2023.
2. Cancer Research UK, Bowel cancer statistics. Accessed July 2023.