

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

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 too¹.

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
Subgroups	If the evidence allows the following subgroups will be considered. These include: <ul style="list-style-type: none"> • People without prior bevacizumab
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 monotherapy • Regorafenib • Nivolumab with ipilimumab (where high microsatellite instability or mismatch repair deficiency is present) • Encorafenib with cetuximab (if BRAF V600E mutation-positive metastatic colorectal cancer) • 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
Economic analysis	<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>
Other considerations	<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.</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.</p> <p>‘Encorafenib plus cetuximab for previously treated BRAF V600E mutation-positive metastatic colorectal cancer’ (2021). NICE Technology Appraisal 668.</p> <p>‘Cetuximab and panitumumab for previously untreated metastatic colorectal cancer’ (2017). NICE Technology Appraisal 439.</p> <p>‘Trifluridine–tipiracil for previously treated metastatic colorectal cancer’ (2016). NICE Technology Appraisal 405.</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.</p> <p>‘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.</p> <p>‘Laparoscopic surgery for colorectal cancer’ (2006). NICE Technology Appraisal 105.</p> <p>‘Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer’ (2003). NICE Technology Appraisal 61.</p> <p>Related appraisals in development (including suspended appraisals):</p> <p>‘Fruquintinib for previously treated metastatic colorectal cancer’. NICE technology appraisals guidance (ID6274). In development.</p> <p>‘Tucatinib with trastuzumab for previously treated HER2-positive colorectal cancer’. NICE technology appraisals guidance (ID6227). In development.</p> <p>‘Pembrolizumab with lenvatinib for previously treated metastatic colorectal cancer’. NICE technology appraisals guidance (ID5112). Appraisal suspended.</p>
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	<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.</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	<p>The NHS Long Term Plan (2019) NHS Long Term Plan</p> <p>NHS England (2018) NHS manual for prescribed specialist services (2018/2019)</p>

References

1. Cancer Research UK, [Bowel cancer statistics](#). Accessed July 2023.