NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Trifluridine in combination with tipiracil hydrochloride for previously treated metastatic colorectal cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of trifluridine in combination with tipiracil hydrochloride within its marketing authorisation for treating metastatic colorectal cancer after standard therapy.

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 most often spreads first to the liver, but metastases may also occur in other parts of the body including the lungs, brain and bones.

In 2012, there were 34,322 people diagnosed with colorectal cancer[1] and 13,236 deaths[2] in England. About 20% to 25% of people with colorectal cancer have metastatic disease when first diagnosed[3,4], and approximately 50% of people who have surgery for early stage disease will eventually develop metastases[5].

Treatment of metastatic colorectal cancer may involve a combination of surgery, chemotherapy, radiotherapy and supportive care. When possible, surgical removal (resection) or destruction of the primary tumour and metastases may be considered.

Treatment for metastatic colorectal cancer aims to prolong survival, improve quality of life and/or make the primary tumour or metastases suitable for resection. Chemotherapy options include: folinic acid plus fluorouracil plus oxaliplatin (FOLFOX), folinic acid plus fluorouracil plus irinotecan (FOLFIRI), capecitabine plus oxaliplatin (XELOX), single-agent irinotecan, capecitabine or tegafur with uracil (in combination with folinic acid) (NICE clinical guideline 131). Chemotherapy may be combined with biological agents such as EGFR inhibitors (cetuximab or panitumumab) or VEGF inhibitors (bevacizumab). If standard therapies are unsuccessful, not tolerated or contraindicated, people are treated with supportive care to manage the symptoms and complications of the condition.

The technology

Trifluridine in combination with tipiracil hydrochloride (Lonsurf, Servier Laboratories) is an anti-cancer treatment comprising a nucleoside analogue and a thymidine phosphorylase inhibitor. The nucleoside analogue

(trifluridine) is incorporated into the DNA of tumour cells and inhibits tumour growth, whereas the thymidine phosphorylase inhibitor (tipiracil hydrochloride) slows the breakdown of trifluridine to prolong its action. It is administered orally as a fixed-dose combination.

Trifluridine in combination with tipiracil hydrochloride does not currently have a marketing authorisation in the UK. It has been studied in clinical trials, compared with placebo, for treating metastatic colorectal cancer in adults for whom 2 or more chemotherapy regimens have failed.

Intervention(s)	Fixed-dose combination of trifluridine and tipiracil hydrochloride
Population(s)	Adults with metastatic colorectal cancer whose disease has progressed after standard therapies or for whom standard therapies are unsuitable
Comparators	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.
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: 'Aflibercept in combination with irinotecan and

and NICE Pathways	fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy' (2014). NICE Technology Appraisal 307. Review date August 2016. 'Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy (review of TA150 and part review of TA118)' (2012). NICE Technology Appraisal 242. Static list. 'Bevacizumab in combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for the treatment of metastatic colorectal cancer' (2010). NICE Technology Appraisal 212. Static list. 'Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer' (2007). Technology Appraisal 118. Guidance on static list. Partially reviewed as part of TA242. Terminated appraisals 'Regorafenib for metastatic colorectal cancer after treatment for metastatic disease' (terminated appraisal) (2015). NICE Technology Appraisal 334. 'Panitumumab in combination with chemotherapy for the treatment of metastatic colorectal cancer' (terminated appraisal) (2011). NICE Technology Appraisal 240. Currently under review [ID794]. Proposed Appraisals 'Ramucirumab in combination with FOLFIRI for treating metastatic colorectal cancer after progression with bevacizumab, oxaliplatin and fluoropyrimidine'. Proposed NICE technology appraisal [ID867]. Publication date to be confirmed. Related Guidelines: 'The diagnosis and management of colorectal cancer' (2011, partially updated December 2014). NICE Guideline CG131. Review date February 2016. Related Quality Standards: 'Colorectal cancer (2012). Quality Standard 20. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: 'Colorectal cancer' (2011). NICE Pathway. http://pathways.nice.org.uk/pathways/colorectal-cancer

Related National Policy	Department of Health, 2013, NHS Outcomes Framework 2014-2015. Domains 1, 2, 4 and 5. Department of Health, 2011, Improving outcomes: a strategy for cancer Department of Health, 2009, Cancer commissioning guidance Department of Health, 2007, Cancer reform strategy NHS England, 2014, Manual for prescribed specialised services 2013/14. Chapter 10. Public Health England, 2011, National Screening Committee policy on bowel cancer screening in adults.

References

1. Office for National Statistics (2012) '10 most common cancers in males and females'. Accessed December 2015.
2. Cancer Research UK (2014) 'Bowel cancer mortality statistics'. Accessed December 2015.
3. Bowel Cancer UK (2015) 'Bowel cancer statistics'. Accessed December 2015.
4. Association of Coloproctology of Great Britain and Ireland (2007) 'Guidelines for the Management of Colorectal Cancer'. Accessed December 2015.
5. Garden OJ, Rees M, Poston GJ et al. (2006) Guidelines for resection of colorectal cancer liver metastases. Gut 55 (Suppl III) iii1–iii8.