NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Atezolizumab for treating locally advanced or metastatic colorectal cancer after 2 therapies

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of atezolizumab within its marketing authorisation for treating locally advanced or metastatic colorectal cancer

Background

Colorectal cancer is a malignant tumour arising from the lining of the large intestine (colon and rectum). Locally advanced means that the cancer has spread to surrounding tissues and 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 2016, there were 34,952 people diagnosed with colorectal cancer and 15,903 deaths in England[1]. About 26% of people with colorectal cancer have locally advanced disease and 22% of people have metastatic disease when first diagnosed[2]. Approximately 50% of people who have surgery for early disease will eventually develop metastases[3].

Treatment for colorectal cancer aims to prolong survival, improve quality of life and/or make the primary tumour or metastases suitable for resection. When surgical resection is not possible, treating with chemotherapy with or without monoclonal antibodies is an option to prolong survival and/or to make the primary tumour or metastases suitable for resection. NICE clinical guideline 131 recommends chemotherapy options including:

- fluorouracil and folinic acid in combination with oxaliplatin (FOLFOX),
- tegafur in combination with fluorouracil and folinic acid,
- capecitabine in combination with oxaliplatin (XELOX), and
- capecitabine alone.

In practice, fluorouracil and folinic acid may also be used in combination with irinotecan (FOLFIRI) in some people for whom oxaliplatin is not suitable. Cetuximab and panitumumab in combination with FOLFOX and FOLFIRI are options for treating RAS wild-type tumours in people with metastatic colorectal cancer (technology appraisal 439). If the initial therapies are unsuccessful, not tolerated or contradicted, the treatment options include: single agent irinotecan, folinic acid plus fluorouracil plus irinotecan (FOLFIRI) or raltitrexed (clinical guideline 131).

NICE technology appraisal 405 recommends trifluridine-tipiracil as an option for treating metastatic colorectal cancer in adults who have had previous treatment with available therapies including fluoropyrimidine-, oxaliplatin- or irinotecan-based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents and anti-epidermal growth factor receptor (EGFR) agents, or when these therapies are not suitable.

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

Atezolizumab (Tecentriq, Roche Products) is a monoclonal antibody which inhibits programmed death-ligand 1 (PD-L1). Inhibition of PD-L1 leads to activation of T cells that can detect and attack tumor cells. It is administered intravenously.

Cobimetinib (Cotellic, Roche Products) is a mitogen-activated extracellular signal related kinase (MEK) inhibitor. Blocking the activity of MEK stops cell proliferation induced by the mitogen-activated protein kinase signalling pathway. It is administered orally.

Atezolizumab in combination with cobimetinib does not currently have a marketing authorisation for treating colorectal cancer. Atezolizumab in combination with cobimetinib and atezolizumab monotherapy has been studied compared with regorafenib in people with unresectable locally advanced or metastatic colorectal cancer, who had at least 2 previous systemic chemotherapy treatments for metastatic disease.

Intervention(s)	Atezolizumab with or without cobimetinib
Population(s)	People with metastatic colorectal cancer who have had 2 previous systemic chemotherapy treatments
Comparators	For people with metastatic colorectal cancer • Trifluridine-tipiracil For people with locally advanced colorectal cancer or for people for whom trifuridine-tipiracil is not suitable • 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 patient access schemes for the intervention or comparator 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 and NICE Pathways	Related Technology Appraisals: Cetuximab and panitumumab for previously untreated metastatic colorectal cancer (2017) NICE technology appraisal guidance 439. Review March 2020 Trifluridine–tipiracil for previously treated metastatic colorectal cancer (2016) NICE technology appraisal guidance 405. Review August 2019 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 guidance 307. On static list Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer (2012) NICE technology appraisal guidance 118. On static list 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 guidance 242. On 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 guidance 212. On static list Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer (2003) NICE technology appraisal guidance 61. On static list Terminated appraisals Panitumumab in combination with chemotherapy for the treatment of metastatic colorectal cancer (terminated appraisal) (2011) NICE technology appraisal guidance 240. Regorafenib for metastatic colorectal cancer after treatment for metastatic disease (terminated appraisal) (2015) NICE technology appraisal guidance 334 Appraisals in development (including suspended appraisals) Nivolumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency [ID1136].Supended Colon cancer (adjuvant) - irinotecan. NICE technology appraisal guidance [ID379] Suspended Pembrolizumab for previously treated metastatic colorectal cancer that has high microsatellite instability or mismatch repair deficiency.NICE technology appraisal guidance [ID1071].Suspended Colorectal cancer (metastatic) - MABp1 (after previous treatment). NICE technology appraisal guidance [ID917] Suspended Nintedanib for previously treated metastatic colorectal cancer. NICE technology appraisal guidance [ID1030]. Suspended Related Guidelines: Colorectal cancer: diagnosis and management (2011) NICE guideline CG131. Review in progress, anticipated publication date October 2019 Improving outcomes in colorectal cancer (2004) NICE guideline CSG5

	Related Quality Standards: Colorectal cancer (2012) NICE quality standard 20 Related NICE Pathways: Colorectal cancer (2012) NICE pathway
Related National Policy	NHS England (2016) 106A. Specialist colorectal surgery services (adults). Manual for prescribed specialised services 2016/17 NHS England (2015) Colorectal Cancer PROMs Report NHS England. A07. Specialised Colorectal Services Department of Health (2016) NHS outcomes framework 2016 to 2017 Domains 1, 4, 5. Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

Questions for consultation

Have all relevant comparators for atezolizumab with or without cobimetinib been included in the scope?

Are there people for whom trifluridine-tipiracil would not be suitable, but would be eligible for atezolizumab? If so, how should this group be defined? How should best supportive care be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom atezolizumab with or without cobimetinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider atezolizumab with or without cobimetinib will fit into the existing NICE pathway, Colorectal cancer?

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 atezolizumab with or without cobimetinib 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.

Do you consider atezolizumab with or without cobimetinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of atezolizumab with or without cobimetinib can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1 Office for National Statistic (2018) Cancer registration statistics England 2016. Accessed January 2018 https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancerregistrationstatisticsengland/2016

2 Cancer Research UK (2018) Bowel cancer incidence statistics. Accessed January 2018 http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bowel-cancer/incidence#heading-Three

3 Garden OJ, Rees M, Poston GJ et al. (2006) Guidelines for resection of colorectal cancer liver metastases. Gut 55 (Suppl III) iii1–iii8