NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Encorafenib with binimetinib for treating advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of encorafenib with binimetinib within its marketing authorisation for treating advanced unresectable or metastatic BRAF V600 mutation-positive melanoma.

Background

Melanoma is a cancer of the skin. In its early stages, melanoma is normally asymptomatic and can often be cured by surgery (resection). However, it can spread or metastasise to nearby lymph nodes (stage III) or to other parts of the body (stage IV). Most melanomas occur in people with pale skin. The risk factors are skin that tends to burn in the sun, having many moles, sun exposure and sunburn.

There were 13,356 new diagnoses of melanoma in England in 2015.[1] Approximately 60% of new diagnoses were in people aged 60 and over.[1] In England in 2012-2015, 7.5% of cases were diagnosed at stage III or IV.[2] There were 1,937 deaths registered in England in 2016.[3]

A mutated form of the BRAF gene is found in 40% to 60% of melanomas; 80% to 90% of these are BRAF V600 mutations.[4] Mutated BRAF genes activate the RAF-MEK-ERK pathway, leading to uncontrolled cell division and growth of the tumour.

Treatment options for advanced melanoma depend on the person's BRAF mutation status and treatment history. In clinical practice, for people with BRAF mutation-positive advanced melanoma, a BRAF inhibitor is the usual first-line treatment. For BRAF V600 mutation-positive unresectable or metastatic melanoma, NICE technology appraisal guidance recommends the BRAF inhibitor, dabrafenib alone (TA321) or with the MEK inhibitor, trametinib (TA396) and the BRAF inhibitor, vemurafenib alone (TA269). Dabrafenib with trametinib is considered the standard of care in clinical practice, replacing the use of targeted BRAF inhibitor monotherapy. NICE technology appraisal guidance 414 does not recommend the use of vemurafenib with the MEK inhibitor, cobimetinib, for treating BRAF V600 mutation-positive advanced melanoma. Immunotherapy is also recommended for advanced melanoma.

The technology

Encorafenib and binimetinib (brand names unknown, Array BioPharma Inc and Pierre Fabre) inhibit the actions of the BRAF V600 gene and MAP kinase 1 and 2 (MEK1/2) respectively, with the aim of slowing the growth and spread of the cancer. Encorafenib and binimetinib are administered orally.

Encorafenib with binimetinib does not currently have a marketing authorisation in the UK for treating advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma. It has been studied in a clinical trial compared with encorafenib or vemurafenib alone, in adults with advanced BRAF V600 mutation-positive melanoma.

Intervention(s)	Encorafenib with binimetinib
Population(s)	Adults with unresectable or metastatic BRAF V600 mutation-positive melanoma
Comparators	Dabrafenib with trametinib
Outcomes	The outcome measures to be considered include: • progression free survival • overall survival • response rate • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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	Where the evidence allows, the following subgroups will be considered: • people with previously untreated disease • people with previously treated disease that progressed on or after first line immunotherapy 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: 'Cobimetinib in combination with vemurafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma' (2016). NICE Technology Appraisal 414. Review date October 2019. 'Trametinib in combination with dabrafenib for treating unresectable or metastatic melanoma' (2016). NICE Technology Appraisal 396. Review date June 2019. . 'Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma' (2014). NICE Technology Appraisal 321. Static list. 'Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma' (2012). NICE Technology Appraisal 269. Static list. Related Guidelines: 'Melanoma: assessment and management' (2015) NICE guideline NG14. Review date to be confirmed. 'Improving outcomes for people with skin tumours including melanoma' (2006) NICE Cancer Service guideline CSG8. Review date March 2018. Related Quality Standards: 'Skin cancer' (2016) NICE quality standard 130. Related NICE Pathways: Melanoma (2016) NICE pathway.
Related National Policy	Department of Health Cancer research and treatment Department of Health (2016) NHS outcomes framework

	2016 to 2017: Domains 1–5. Department of Health (2014) The national cancer strategy: 4th annual report NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Chapter 105. Specialist cancer services (adults). NHS England (2013) NHS standard contract for cancer: skin (adult) A12/S/b.

References

1. National Cancer Registration and Analysis Service. Routes to diagnosis 2006-2016 workbook (a). Accessed June 2018.

2. National Cancer Registration and Analysis Service. Routes to diagnosis 2006-2016 workbook (b). Accessed June 2018.

3. Cancer Research UK (2014) Skin cancer statistics. Accessed June 2018.

4. Vora NL. (2016) Melanoma and BRAF. Medscape. Accessed January 2018.