NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Dabrafenib for treating unresectable, advanced or metastatic BRAF^{V600} mutation-positive melanoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dabrafenib within its licensed indication for the treatment of unresectable, advanced or metastatic BRAF^{V600} mutation-positive melanoma.

Background

Melanoma is a type of skin cancer which in its early stages is normally asymptomatic and, if detected early, before it has spread, can be curable by resection. However, at presentation, around 10% of melanomas will have metastasised. Melanoma can spread to nearby lymph nodes (stage III, of which stage IIIc disease includes tumours of varying size with extensive lymph node involvement but no metastases) or to other parts of the body (stage IV). It occurs more commonly in fair-skinned people and there is strong evidence that ultra violet exposure is causal. People with an above-average mole count, sun-sensitive skin, or a strong family history of melanoma are at greatly increased risk.

The incidence of melanoma is increasing in England with rates doubling approximately every 10-20 years. There were 10,656 new diagnoses of melanoma in 2010 and 1871 deaths registered in the England in 2010. In the UK, melanoma is diagnosed at a mean age of around 50 years but approximately 20% of cases occur in young adults aged between 15 and 39 years old. Five-year survival rates are approximately 20-30% for stage IIIc disease and approximately 7-20% for stage IV disease.

BRAF is part of the RAS/MAPK signalling pathway, which helps to control cell proliferation, differentiation and death. Companion diagnostic tests can be used to detect the BRAF mutation, including the cobas test, generic PCR sequencing tests and other validated BRAF mutation tests. The mutated form BRAF^{V600} is found in approximately 50% of melanomas.

Early recognition of melanoma and accurate diagnosis presents the best opportunity for cure by surgical resection of the tumour. A very small minority of people with advanced disease can still have their tumour removed. First-line treatment for people with a BRAF^{V600} mutation is normally vemurafenib, but dacarbazine and ipilimumab are also treatment options. Radiotherapy, immunotherapy and combination chemotherapy have also been studied in randomised clinical trials.

NICE technology appraisal No. 269 recommends vemurafenib as an option for treating $BRAF^{V600}$ mutation-positive unresectable or metastatic melanoma only if the manufacturer provides vemurafenib with the discount agreed in the patient access scheme. NICE technology appraisal No. 268 recommends ipilimumab as an option for treating advanced (unresectable or metastatic) melanoma in people who have received prior therapy, only if the manufacturer provides ipilimumab with the discount agreed in the patient access scheme. A NICE technology appraisal of ipilimumab for previously untreated unresectable stage III or IV melanoma is currently ongoing.

The technology

Dabrafenib (Tafinlar, GlaxoSmithKline) is a selective ATP-competitive BRAF (serine/threonine-protein kinase BRAF) inhibitor. When the activity of mutant protein kinase is blocked, the cancer cells stop growing and die. It is administered orally.

Dabrafenib has a UK marketing authorisation for monotherapy in the treatment of adult patients with unresectable or metastatic melanoma with a $BRAF^{V600}$ mutation.

Intervention(s)	Dabrafenib
Population(s)	People with advanced or metastatic $BRAF^{V600}$ mutation-positive melanoma
Comparators	For people with previously untreated melanoma: • dacarbazine (or temozolomide for people whose melanoma has metastasised to the brain) • vemurafenib For people with previously treated melanoma: • dacarbazine (or temozolomide for people whose melanoma has metastasised to the brain) • ipilimumab • vemurafenib
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. 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 should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Cost of any additional mutational testing required for this treatment should be considered.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 268, December 2012, 'Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma'. Review decision date November 2014. Technology Appraisal No.269, December 2012, 'Vemurafenib for treating locally advanced or metastatic $BRAF^{V600}$ mutation-positive malignant melanoma'. Review decision date November 2014. Technology Appraisal in Preparation, 'Ipilimumab for previously untreated unresectable melanoma'. Earliest anticipated date of publication July 2014. Technology Appraisal in Preparation, 'Paclitaxel formulated as albumin-bound nanoparticles for the first-line treatment of metastatic melanoma'. Earliest anticipated date of publication June 2015. Related clinical guidelines: Clinical Guideline in Preparation, 'Melanoma: assessment and management of melanoma'. Earliest anticipated date of publication TBC.
Related National Policy	None