NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Dabrafenib with trametinib for treating BRAF V600E mutation-positive glioma in children and young people

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of dabrafenib with trametinib within its marketing authorisation for treating BRAF V600E mutation-positive glioma in children and young people.

Background

Gliomas are the most common type of primary brain tumour. They develop from the glial cells that support the nerve cells of the brain and spinal cord. In the NHS gliomas are graded according to the most recent World Health Organisation (WHO) categories which take account of likely growth rate. Grade 1 or 2 tumours are considered 'low-grade', are slow growing and may rarely spread to other areas of the brain. Grade 3 and 4 tumours, known as 'high-grade', are malignant and have a worse prognosis. The types of glioma are further identified by the cells they develop from (astrocytoma, ependymoma and oligodendroglioma) and increasingly, by a range of genetic markers including BRAF mutation status.[1]

The symptoms of glioma in children and young people are often general and non-specific and may include headaches, nausea or vomiting, double vision and seizures. Other symptoms depend on where the glioma is in the brain.[2] Glioma is associated with wide reaching impacts on quality of life, including loneliness, difficulty doing activities outside the house and difficulty concentrating and processing information[3]. In children and young people there are around 150[4] diagnoses of low-grade glioma and around 30[5] diagnoses of high-grade glioma each year in the UK. It is estimated that around 7 to 20% of glioma in children and young people has a BRAF V600E mutation.[1,6] Low-grade glioma has a better prognosis than high-grade glioma. 5-year survival rates for grade 1 glioma is around 95% and for grade 2 glioma is around 40 to 50%. High-grade glioma has a lower 5-year survival rate, at 25 to 30% for grade 3 glioma and 5 to 10% for grade 4 glioma.[7]

Treatment for glioma depends on the grade of the tumour, where the tumour is in the brain, if it is possible to remove the tumour with surgery, age and if symptoms are present. Low-grade glioma is usually treated with surgery if possible, which may achieve either complete or partial macroscopic resection of the tumour. After surgery, radiotherapy or proton beam therapy, with or without chemotherapy may be used. Chemotherapy may also be used alone. High-grade glioma is also usually treated with surgery. Depending on age, some children and young people may be given radiotherapy with or without chemotherapy after surgery. Some children may be given chemotherapy only.

The technology

Dabrafenib (brand name unknown) with trametinib (brand name unknown; both Novartis) does not currently have a marketing authorisation in the UK for treating BRAF V600E mutation-positive glioma. It has been studied in a clinical trial of

children and young people aged 1 to 17 years with low-grade glioma that requires systemic treatment following surgery or that cannot be surgically resected and high-grade glioma that has been previously treated. People with low-grade glioma were randomised to receive either dabrafenib with trametinib or vincristine with carboplatin. People with high-grade glioma all received dabrafenib with trametinib.

Intervention	Dabrafenib with trametinib
Population	Children and young people with BRAF V600E mutation-positive glioma
Subgroups	• Low-grade glioma that requires systemic treatment • High-grade glioma that has relapsed, progressed or failed to respond to previous systemic treatment
Comparators	For children and young people with low-grade glioma: • Chemotherapy (including but not limited to vincristine with carboplatin) For children and young people with high-grade glioma: • Chemotherapy • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • duration of response • adverse effects of treatment • health-related quality of life (of patients and carers)

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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The use of dabrafenib with trametinib is conditional on the presence of BRAF V600E mutation. The economic modelling should include the costs associated with diagnostic testing for BRAF V600E in people with glioma who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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:** Guidance on the use of temozolomide for the treatment of recurrent malignant glioma (brain cancer) (2001) NICE technology appraisal guidance 23. **Related technology appraisals in development:** DCVax-L for treating newly diagnosed glioblastoma multiforme. NICE technology appraisal guidance [ID836] Publication date to be confirmed. **Related NICE guidelines:** Brain tumours (primary) and brain metastases in over 16s (2018) NICE guideline NG99. **Related interventional procedures:** Photodynamic therapy for brain tumours (2009) NICE interventional procedures guidance 290 **Related quality standards:** Brain tumours (primary) and brain metastasis in over 16s (2021) NICE quality standard 203

Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019). Chapter 106: Specialist cancer services for children and young people.

References

1. Andrews, Lily J., et al. Prevalence of BRAF V600 in glioma and use of BRAF Inhibitors in patients with BRAF V600 mutation-positive glioma: systematic review. *Neuro-oncology* 24.4 (2022): 528-540.

2. Cancer Research UK; Astrocytoma in children. Accessed July 2023

3. The Brain Tumour Charity; Losing my place: the reality of childhood with a brain tumour. Accessed July 2023

4. The Royal Marsden NHS Foundation Trust; Low grade glioma. Accessed July 2023

5. The Royal Marsden NHS Foundation Trust; High grade glioma. Accessed July 2023

6. Nobre L, et al. Outcomes of BRAF V600E Pediatric Gliomas Treated With Targeted BRAF Inhibition. JCO Precis Oncol. (2020) May 20

7. Brain Tumour Research; Glioma. Accessed July 2023