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 aged 1 to 17

Draft scope

Draft 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 aged 1 to 17.

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' and usually classed as benign or non-cancerous, although they may transform into malignant tumours. 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] In children and young people there are around 150[3] diagnoses of low-grade glioma and around 30[4] diagnoses of high-grade glioma each year in the UK. It is estimated that around 7% of glioma in children and young people has a BRAF V600E mutation.[1] 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.[5]

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 (for children and young people aged 10 years and older) 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. For children and young people aged 3 years and older, radiotherapy with or without chemotherapy is used after surgery. For children under 3 years, surgery is usually followed by chemotherapy only.[2]

The technology

Dabrafenib (Tafinlar) with trametinib (Mekinist; 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 carboplatin with vincristine. People with high-grade glioma all received dabrafenib with trametinib.

Intervention	Dabrafenib with trametinib
Population	Children and young people aged 1 to 17 years 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	• Chemotherapy • 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 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.

Questions for consultation

Where do you consider dabrafenib with trametinib will fit into the existing care pathway for i) low-grade glioma and ii) for high-grade glioma?

Which treatments would dabrafenib with trametinib replace? Would it be used instead of or alongside radiotherapy or proton beam therapy, for example?

Does treatment vary according to age? If yes, which treatments are used for different age ranges?

Which chemotherapy drugs are used for treatment of low-grade and high-grade glioma in children and young people?

How many children and young people with glioma would be eligible for dabrafenib with trametinib in England? Are there any recent prevalence studies or other appropriate data sources which provide a reliable estimate of the prevalent population?

Is there unmet need for new treatments for i) low grade-glioma and ii) high-grade glioma?

Is it anticipated that dabrafenib with trametinib will offer significant additional benefit over current treatments for i) low-grade glioma and ii) high-grade glioma?

Would dabrafenib with trametinib be a candidate for managed access?

Do you consider that the use of dabrafenib with trametinib can result in any potential 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 committee to take account of these benefits.

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 dabrafenib with trametinib 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

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 April 2023

3. The Royal Marsden NHS Foundation Trust; Low grade glioma. Accessed April 2023

4. The Royal Marsden NHS Foundation Trust; High grade glioma. Accessed April 2023

5. Brain Tumour Research; Glioma. Accessed April 2023