NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

DCVax-L for treating newly diagnosed glioblastoma multiforme

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of DCVax-L for newly diagnosed glioblastoma multiforme.

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. There are 3 main types of gliomas, named according to the cells they develop from: astrocytoma, ependymoma and oligliodendroglioma. Gliomas are graded according to their likely growth rate, from grade 1 (slowest growing) to grade 4 (fastest growing). Grade 1 and 2 tumours are considered 'low-grade', with grade 1 tumours usually classed as benign or non-cancerous. Grade 3 and 4 tumours, known as 'high-grade', are malignant and have a worse prognosis. Glioblastoma multiforme, usually grade 4 glioma, is the most common type of astrocytoma and is the most aggressive type of brain tumour.

The most recent World Health Organisation (WHO) classifications of central nervous system tumours sub-divides glioblastoma multiformes in to three groups that reflect both the histology and the molecular genetic changes in the isocitrate dehydrogenase (IDH) genes as follows: glioblastoma multiforme, IDH-wildtype (incorporating giant-cell glioblastoma, gliosacoma and epitheliod glioblastoma); glioblastoma multiforme, IDH-mutant; glioblastoma multiforme not otherwise specified (NOS)[1].

Symptoms of glioblastoma multiforme depend on the size, location, and degree of infiltration of the tumour. They include headache, nausea, vomiting, seizure, visual disturbance, speech and language problems and changes in cognitive or functional ability which can impact on activities of daily living such as washing, dressing, eating and mobility. Scales of performance status, such as the WHO performance status, can be used to categorise functional ability with glioblastoma multiforme.

In 2015, approximately 2500 people were diagnosed with glioblastoma multiforme in England[2]. Between 2010 and 2011, 40% of adults with brain cancer in England and Wales survived for 1 year or more and 19% survived for 5 years or more[3].

Treatment usually consists of surgical resection if possible, which may achieve either complete or partial macroscopic resection of the tumour,

although complete resection is rare. After surgery, radiotherapy with or without chemotherapy is used. If the size or position of the tumour mean surgery is not appropriate, radiotherapy and/or chemotherapy is offered. NICE technology appraisal guidance 121 recommends temozolomide as an option for treating newly diagnosed glioblastoma multiforme in people with a WHO performance status of 0 or 1. It also recommends carmustine implants for newly diagnosed high-grade glioma, but only for people in whom 90% or more of the tumour has been resected. Both temozolomide and carmustine implants are licensed in combination with radiotherapy.

The technology

DCVax-L (Northwest Biotherapeutics) stimulates the immune system and enables patients T-cells and antibodies to recognise and destroy the tumour. This is derived from the patient's own tumour tissue (which provides the antigenic component of the therapy) and precursor dendritic cells which are cultured into mature dendritic cells. DCVax-L is administered by intra-dermal injection.

DCVax-L does not currently have a UK marketing authorisation for treating glioblastoma multiforme. It is being studied in a placebo-controlled clinical trial in adults with newly diagnosed glioblastoma multiforme who have had surgical resection followed by radiotherapy and temozolomide. It is also being studied in phase I/II clinical trials for treating people with both low and high grade gliomas.

Intervention(s)	DCVax-L treatment with radiotherapy and temozolomide
Population(s)	People with newly diagnosed glioblastoma multiforme who have had surgical resection and radiotherapy and are currently receiving temozolomide
Comparators	Standard of care without DCVax-L
Outcomes	The outcome measures to be considered include: • overall survival • progression-free 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If the evidence allows, the appraisal will identify subgroups for whom treatment may be particularly appropriate.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** 'Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma' (2007) NICE technology appraisal 121. Added to static list March 2016. **Related guidelines**: 'Improving outcomes for people with brain and other central nervous system tumours' (2006). Cancer service guideline 10. Review date to be confirmed. *Guideline in development* Primary brain tumours and cerebral metastases. NICE clinical guideline. Publication expected July 2018. **Related Interventional Procedures:** 'Photodynamic therapy for brain tumours' (2009) NICE interventional procedures guidance 290. **Related NICE Pathways**: Brain cancers (2016) NICE Pathway http://pathways.nice.org.uk/pathways/brain-cancers
Related National Policy	National Service Frameworks: Cancer NHS England (2013) Cancer: Brain and Central Nervous System Service Specifications Department of Health (2014) NHS outcomes framework 2015-2016 Department of Health (2011) Improving outcomes: a

	strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

References

1. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol. 2016 Jun;131(6):803-20.

2. Cancer Research UK 'Brain, other CNS and intracranial tumours incidence statistics'. Accessed March 2018.

3. Cancer Research UK 'Brain, other CNS and intracranial tumours survival statistics'. Accessed March 2018.

4. Stupp et al (2005); N Engl J Med;352(10):987-96