NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA121; Carmustine implants and temozolomide for the treatment of newly diagnosed high grade glioma

This guidance was issued in June 2007
The current review date for this guidance is August 2010

Recommendation

- The decision to review the guidance should be deferred until 2015 that we consult on the proposal.

Consideration of options for recommendation:

Options	Comment
A review of the guidance should be planned into the appraisal work programme.	No evidence to suggest a review is necessary at this stage
The decision to review the guidance should be deferred until 2015	**There are ongoing studies identified that would suggest an appropriate review date.**
A review of the guidance should be combined with a review of a related technology and conducted at the scheduled time for the review of the related technology.	No related technology
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	No related appraisal
A review of the guidance should be incorporated into an on-going clinical guideline.	No relevant guideline
A review of the guidance should be updated into an on-going clinical guideline.*[1]	No relevant guideline
A review of the guidance should be transferred to the 'static guidance list'.	No new evidence

Original remit(s)

To appraise the clinical and cost effectiveness of carmustine implants for the treatment of recurrent glioblastoma multiforme (GBM) and newly diagnosed

[1] See Appendix A on page 4

high-grade malignant glioma as an adjunct to surgery and radiation and to appraise the clinical and cost effectiveness of temozolomide within its licensed indications for glioblastoma multiforme (GBM) as an adjunct to surgery and radiation.

Current guidance

Temozolomide and carmustine implants have been appraised separately for the treatment of newly diagnosed high-grade glioma. On the basis of the evidence presented to the Committee, no recommendation can be made regarding the sequential use of these treatments for newly diagnosed high-grade glioma.

1.1 Temozolomide, within its licensed indications, is recommended as an option for the treatment of newly diagnosed glioblastoma multiforme (GBM) in patients with a World Health Organization (WHO) performance status of 0 or 1.

1.2 Carmustine implants, within their licensed indications, are recommended as an option for the treatment of newly diagnosed high-grade glioma only for patients in whom 90% or more of the tumour has been resected.

1.3 Treatment with carmustine implants should be provided only within specialist centres that in general conform to guidance in 'Improving outcomes for people with brain and other central nervous system tumours' (NICE cancer service guidance 2006; www.nice.org.uk/csgbraincns), and should be supervised by specialist neurosurgeons who spend at least 50% of their clinical programmed activities in neuro-oncological surgery. The specialists should also have access to:

- multidisciplinary teams to enable preoperative identification of patients in whom maximal resection is likely to be achievable
- magnetic resonance imaging (MRI) to enable preoperative identification of patients in whom maximal resection is likely to be possible, and
- image-directed technology, such as neuronavigation, for use intraoperatively to assist the achievement of maximal resection.

1.4 Carmustine implants are not recommended for the treatment of newly diagnosed high-grade glioma for patients in whom less than 90% of the tumour has been resected.

Relevant Institute work

Published

Cancer service guidance CSGBraincns. Service guidance for improving outcomes for people with brain and other central nervous system tumours. Issued: June 2006. Expected review date: TBC

Technology Appraisal TA23 Temozolomide for the treatment of recurrent malignant glioma (brain cancer). Published: April 2001. A review was proposed in 2006 but it has not been updated as of July 2010 (awaiting results of a clinical trial).

IPG Number: IPG290 Photodynamic therapy for brain tumours. Guidance issue date: 5 March 2009

Suspended/terminated

Technology appraisals TA149 Carmustine implants for the treatment of recurrent glioblastoma multiforme. Issued: June 2008. Guidance terminated in June 2008 because insufficient evidence was provided by the manufacturer.

Technology appraisal. Bevacizumab for the treatment of recurrent glioblastoma. The Committee for Medicinal Products for Human Use (CHMP) recently adopted a negative opinion on extending the current indication of bevacizumab (Avastin) to include use in patients with recurrent glioblastoma. NICE has therefore decided to remove this appraisal from its current work programme.

In topic selection

[redacted]

On-going trials

Trial name and contact	Details
Radiation Therapy Combined With Chemotherapy in Treating Patients With Anaplastic Astrocytoma or Mixed Gliomas (NCT00004259)	This randomized phase III trial is studying radiation therapy and temozolomide to see how well they work compared to radiation therapy and carmustine IV or lomustine IV in treating patients with anaplastic astrocytoma or mixed gliomas.

	Estimated Enrollment: 474 Estimated Primary Completion Date: N/A No completion date
Radiation Therapy or Radiation Therapy and Temozolomide or Temozolomide Alone in Treating Patients With Newly Diagnosed Anaplastic Glioma (NCT00887146)	This randomized phase III trial is comparing giving temozolomide alone, radiation therapy alone, or temozolomide together with radiation therapy to see which works best in treating patients with newly diagnosed anaplastic glioma. Estimated Enrollment: 488 Estimated Primary Completion Date: February 2014
Radiation Therapy With or Without Temozolomide in Treating Patients With Anaplastic Glioma (NCT00626990)	This randomized phase III trial is studying giving temozolomide during and/or after radiation therapy to see how well it works compared with radiation therapy alone in treating patients with anaplastic glioma. Estimated Enrollment: 748 Estimated Primary Completion Date: June 2015
Temozolomide Compared to Procarbazine, Lomustine, and Vincristine in Treating Patients With Recurrent Malignant Glioma (NCT00052455)	Randomized phase III trial to compare the effectiveness of temozolomide alone to that of procarbazine, lomustine, and vincristine in treating patients who have recurrent malignant glioma. Estimated Enrollment: 500 No completion date.
Standard Temodal (Temozolomide) Regimen Versus Standard Regimen Plus Early Postsurgery Temodal for Newly Diagnosed Glioblastoma Multiforme (Study P05572) (NCT00686725)	The primary purpose of the study is to evaluate the efficacy and safety of early postsurgery temozolomide chemotherapy followed by the standard temozolomide regimen, compared to the standard regimen alone, for the treatment of patients with newly diagnosed glioblastoma multiforme. Estimated Enrollment: 100 Estimated Study Completion Date: September 2011
Efficacy and Safety Study of Lomustine/Temozolomide Combination Therapy vs. Standard Therapy for Glioblastoma Patients (CeTeG) (NCT01149109)	Phase III Trial of CCNU/Temozolomide (TMZ) combination therapy vs. standard TMZ Therapy for Newly Diagnosed MGMT-methylated glioblastoma patients. Estimated Enrollment: 128

	Estimated Study Completion Date: February 2015
Radiation Therapy With or Without Temozolomide in Treating Older Patients With Newly Diagnosed Glioblastoma Multiforme (NCT00482677)	This randomized phase III trial is studying radiation therapy and temozolomide to see how well it works compared with radiation therapy alone in treating patients with newly diagnosed glioblastoma multiforme. Estimated Enrollment: 560 Estimated Study Completion Date: December 2012

Proposal for updating the guidance

If the guidance is to be updated as an appraisal, it would be scheduled into the work programme accordingly.

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline(R) In-Process and Embase. References from 2005 onwards were reviewed. The results of the literature search are discussed in the 'Appraisals comment' section below.

Implementation

No submission was received from Implementation.

Equality and diversity issues

No equality and diversity issues have been identified.

Appraisals comment:

The updated literature searches identified six new studies comparing temozolomide and radiotherapy with radiotherapy alone. The studies demonstrated a survival benefit for the combination of radiotherapy with temozolomide compared with radiotherapy alone. These study results support the original conclusions of technology appraisal 121.

Another study looked at the cost-effectiveness of temozolomide and concluded that despite the high temozolomide acquisition costs, the costs per life-year gained were comparable with accepted first-line treatment with chemotherapy.

The literature search also identified a study that examined the safety profile of carmustine implants and concluded that the adverse event rate reported in the

current treatment strategies was comparable to those observed in the initial registration studies.

No evidence on the sequential use of temozolomide and carmustine implants was identified.

Generic formulations of temozolomide became available in 2010. However this is unlikely to change in the recommendations as temozolomide was considered to be a cost-effective use of NHS resources before generic alternatives were available.

This new evidence does not suggest that the recommendations would change if the appraisal was subject to review. Given that there are relevant trials due to report by 2014/15 a review of the guidance should be deferred until these trials have completed.

Key issues

No new evidence has emerged that would necessitate a review of this guidance at this point and we therefore suggest that the review is deferred until 2015.

GE paper sign off: Elisabeth George 28 07 10

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