Submission from CancerBACUP to NICE Appraisal Committee on carmustine implants and temozolomide for the treatment of newly diagnosed high grade glioma

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CancerBACUP welcomes the opportunity to contribute to the appraisal of carmustine implants and temozolomide for the treatment of newly diagnosed high grade glioma. As the leading specialist provider of independent information on all types of cancer, CancerBACUP has regular contact with people living with high grade gliomas and those caring for them.

CancerBACUP received nearly 1,611 enquiries between April 2003 and March 2004 from people affected by brain tumours.

CancerBACUP believes that everyone with cancer should be offered the most effective and appropriate treatment, based on the available evidence and the patient's own wishes and preferences. We believe that:

- Patients should have access to the most effective treatments appropriate to them as individuals;
- Patients should be able to choose – in partnership with their oncologist – the treatment that is likely to suit them best in terms of relative benefits and side-effects;
- The impact of treatments on patient's quality of life, as well as length of life, should be given full consideration by the Appraisal Committee.

We urge the Appraisal Committee to recommend that carmustine implants and temozolomide should be made available for patients for the treatment of newly diagnosed high grade glioma.

Living with high grade glioma

An estimated 3,960 brain tumours were diagnosed in England and Wales in 2002.[1] In the early stages, brain tumours most commonly cause headaches and feeling sick. These symptoms are usually caused by a rise in the pressure within the brain as the tumour grows. The rise in pressure is called *raised intracranial pressure.*

[1] CancerStats Monograph 2004, Cancer Research UK

Different types of brain tumours are usually named after the types of brain cells from which they have developed. Some tumours develop from the supporting cells of the brain known as the glial cells. They may be named after they type of cell that they are made up of, or after the part of the brain in which they are found, such as a brainstem glioma. More than half of all primary brain tumours are gliomas.

Grading of gliomas

There are four grades of glioma. Grading is usually carried out by pathologist and gives an idea of how quickly the tumour may develop.

There are four grades: grade 1 tumours are the least malignant and grow only very slowly, whereas grade 4 tumours are more malignant and grow faster. Sometimes grade 1 and 2 gliomas are called low-grade gliomas and grades 3 and 4 are called high grade gliomas.

Treatment for high grade glioma

Surgery, radiotherapy or chemotherapy may be used alone or in combination to treat brain tumours.

Carmustine implants

Carmustine implants are thin absorbable sheets of material containing carmustine chemotherapy. During surgery, the wafers are put into the area of the brain where the tumour has been removed.

Temozolomide

Temozolomide is a chemotherapy drug that is given as a treatment for some types of brain tumour. It is most commonly used to treat higher grade gliomas.

CancerBACUP argues strongly that NICE should recommend that carmustine implants and temozolomide are available on the NHS for the treatment of patients with high grade glioma in accordance with their licences for the following reasons:

1. **Carmustine implants and temozolomide can extend survival**

Results of a recent phase III study concluded that carmustine implants significantly prolongs survival and time to relapse in patients having initial resective surgery for malignant glioma followed by radiotherapy.[2]

[2] A phase III trial of local chemotherapy with biodegradable carmustine (BCNU) wafers (Gliadel wafers) in patients with primary malignant glioma: Westphal M, Hilt DC, Delavault P, Olivares R, Warnke P C, Whittle I R, Jaaskelainen J, Ram Z; Neuro-Oncology, 2003, 5/2 (79-88)

Two hundred and forty patients were randomized to receive either carmustine (BCNU) or placebo wafers at the time of primary surgical resection. Both groups were treated with external beam radiation postoperatively. The two groups were similar for age, sex, Karnofsky performance status and tumour histology. Median survival in the intent to treat group was 13.9 percent for the carmustine implant group and 11.6 months for the placebo–treated group, with a 29 percent reduction in the risk of death in the treatment group.

The efficacy of temozolomide has also been demonstrated in both pre-clinical and phase I and II studies.[3] Forty-two patients with newly diagnosed gliobastoma, anaplastic astrocytoma and anaplastic oligodendroglioma. The mean follow-up period was 12 months. The overall response rate (only responsive patient) for all histological groups was 40 percent, 10 patients (24 percent) showed a stabilization of disease. The median progression free survival and overall survival was respectively 8.35 and 14.1 months. Time to progression was 34 week ranging from 21 to 47.

2. **Temozolomide can improve survival while improving patients' quality of life**

In a phase I trial, temozolomide was administered to patients concomitantly with radiotherapy. In phase II of the trial, twenty-one patients with newly diagnosed glioblastoma were enrolled four weeks after completion of radiotherapy. Each patient was administered a monochemotherapy using temozolomide.[4]

The one-year survival rate of patients was 58 percent and median survival time was 15.7 months. Both phases of the trial were well tolerated. Nonhaematological adverse events were rare and mild to moderate in severity. Grade 3 and 4 neutropenia and thromocytopenia were the only significant haematological side effects observed in only three patients in phase I and four patients in phase II of the trial.

Declaration of interest

CancerBACUP has received sponsorship from Schering Plough, the manufacturer of temozolomide for several publications and projects.

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[3] Temozolomide as a first-line agent in treating high-grade gliomas: phase II study: Chibbaro S, Benvenuti L, Caprio a, Carnesecchi S, Purlera F, Faggionato F, Serion D, Galli C, Andreuccetti M, Buxton N, Gagliardi R; Journal of neuro-oncology; Mar-Apr 2004, vol.67, no.1-2, p 77-81

[4] Temozolomide in radio-chemotherapy combined treatment for newly diagnosed glioblastoma multiforme: phase II clinical trial: Lanzetta G, Campanella C, Rozzi A, Nappa M, Costa A, Fedele F, Innocenzi G, Gagliardi F M, Salvati M, Minniti G, Frati L, Vecchione A; Anticancer research; Nov-Dec 2003; no 6D, p 5159-64