Appraisal of carmustine implants and temozolomide for newly diagnosed high grade glioma

Brain and Spine Foundation

January 2006

Submission to the National Institute for Health and Clinical Excellence

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Putting the patient first

The Brain and Spine Foundation strongly challenges the recommendations proposed by the committee, namely that temozolomide and carmustine implants should not be recommended for people newly diagnosed with high grade glioma.

Only passing reference is made to the patient perspective in the ACD and the issues specific to patients with high grade glioma's are not considered. NICE currently adopts utility values based on those of a panel of people who are asked to envisage what a condition is like to have. We argue that it is impossible for someone to imagine what it is like for a person, often with young children, to be given the diagnosis of a high grade glioma. There is no other cancer which can potentially affect some many aspects of a person's life (cognitive, physical and psychological), or indeed the very essence of their self. It is impossible to imagine what value these people and their families place on increasing the lives by a few months. The chance of a treatment (without any detriment in quality of life) is priceless, but society at large may find it hard to comprehend this.

A recent audit revealed that every call to our helpline on high grade glioma involved a request for further information about clinical trials or treatment options. Our experience on the helpline and from consulting with people, including children, affected by brain tumours has clearly indicated that they want the treatments under consideration here to be made available on the NHS. It is unacceptable that they will only be available on an ability-to-pay basis or only in those parts of the country where clinicians are able to fund clinical trials thus maintaining the postcode lottery that NICE was originally established to redress.

In general, NICE considers a treatment costing less than £20,000 per QALY as cost effective. We argue that this discriminates against conditions such as high grade gliomas because they have a low incidence and a poor prognosis. It will be many years before a treatment will be developed that will add years to a person's life and not just months. NICE will reject all of these treatments, not because they are ineffective but because their model is inappropriate.

Specific Comments

Section 1

1.3 We challenge the recommendations made for further clinical studies on these treatments:

- Quality of life has already been assessed in a study by Taphoorn et al (2005). Quality of life was assessed using reliable and valid measures, namely the European Organsiation for Research and Treatment for Cancer (EOTRC) quality of life questionnaire (QLQ-C30) and the EORTC brain cancer module (EOTRC BN-20). It is highly improbable that any additional funding will be secured to investigate this is more detail, especially in the UK, if these treatments are not recommended.

- The MGMT trial is already in progress. The committee highlight the apparent importance of MGMT status, however this alone is unlikely to predict response to temozolomide. We already know that the extent of resection and performance status do predict response survival time.

Section 2

We would like to emphasis the number of life years lost rather than the incidence of this particular cancer. Burnet et al (2005) calculated years of life lost, a population-based mortality indicator, across different cancer sites. Brain and CNS tumours are calculated to have the highest number of average

life year lost, namely 20.1 yrs, out of all the cancer sites. Despite this, it only attracts 1.5% of the National Cancer Research Institute spending.

Section 3
No comment

Section 4
4.1.4 and 4.1.10

Throughout the report emphasises the median survival data detracting attention away from the long term survival advantage gained from these treatments. For example, in the Stupp et al (2005) trial the 18 month survival rates for radiotherapy plus temozolomide are 39.4% compared to 20.9% for radiotherapy only. Furthermore,
an increase survival of 3 months for someone who may only live for 12 months is a 25% increase. The economic model should reflect the proportionate, and not the absolute, increase in survival time

4.1.11
MGMT status may be a predictor of response to temozolomide but this is yet to be established. It is not a basis on which to defer i.e. wait until a review, before deciding whether to fund this treatment on the NHS. The existing data already indicate which clinical factors predict response to treatment.

4.1.12
The existing data already indicates which sub groups of patients will benefit from the treatment. The numbers are small but this is likely to be a problem for any treatment involving such a patient population.

4.3.1

The economic model seems to be particularly sensitive to relatively small changes in certain parameters. The values that have been used are very much open to question. Given the challenges made by several well respected clinicians about the use of this model, we seek further clarification on its validity and robustness.

The committee note that the characteristics of the trial populations do not match those of the general patient population which limits the findings. However, in clinical practice these treatments would not be offered to patients with a low performance score or where surgery is not possible or indicated. Thus we argue that the trials population is representative of the patients who would be offered these treatments. The total cost to the NHS would therefore be significantly less than quoted.

Section 9

Why was 2009 chosen as the review date? Was this decision based on when further clinical trial data is expected to be available?

Summary

- It appears that NICE has adopted one model and one process, irrespective of the condition or the type of treatment under consideration. One size does not fit all.

- Temozolomide and carmustine implants represent the first effect treatments for high grade gliomas in many years.

- These treatments are highly valued by clinicians. Clinicians want to prescribe these treatments for a sub-group of patients and their submissions support their efficacy.

- Both patients and clinicians are extremely concerned about the possibility that these treatments will not be made available. This decision will have far reaching ramifications for the brain tumour community and will severely impede research in this country.

References

N G Burnet, S J Jefferies, R J Benson, D P Hunt and F P Treasure. (2005). Years of life lost (YLL) from cancer is an important measure of population burden - and should be considered when allocating research funds *British Journal of Cancer* 92, 241-245.

M J Taphoorn, R Stupp, C Coens, D Osoba, R Kortmann et al (2005). *Lancet Oncology* 6(12):937-44