SAMANTHA DICKSON RESEARCH TRUST

FINDING A CURE FOR BRAIN TUMOURS

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Dear Sirs

We are attaching our response to the Appraisal Consultation Document: Glioma (newly diagnosed and high grade) – carmustine implants and temozolomide.

As the leading brain tumour charity in the UK, we were dismayed to read your recommendations made in the consultation document. We represent the voice of many hundreds, if not thousands, of brain tumour patients throughout the UK and we are constantly receiving complaints in relation to the fact that Temozolomide is not available to all patients.

We were hoping that the recommendations would improve this situation but it seems at the moment that the opposite is true and that the situation is likely to worsen.

What we also find disturbing is that, after detailed analysis of your appraisal, we can find no scientific, clinical or statistical justification for your recommendations.

Yours faithfully

[redacted]

Angela and Neil Dickson

SDRT's response to Appraisal Consultation Document: Glioma (newly diagnosed and high grade) – carmustine implants and temozolomide

Section 1 : Preliminary recommendations

These preliminary recommendations are not acceptable as:

- The quality of life has already been assessed (Tapphorn's study) and found that temozolomide maintains the quality of life
- The MGMT trial is already in progress
- Subgroup analysis is already incorporated into currently running studies
- Comparison of temozolomide or carmustine implants with other chemotherapy regimens suggests that these treatments have already been accepted as the standard of care. NICE have not recommended these agents for the treatment of newly diagnosed high grade glioma.

Section 2 : Clinical need and practice

- There is a lack of data on Person Life Years of Life Lost (YLL) with regard to brain tumours. I quote from Dr Burnett's study publishes in the British Journal of Cancer (2005) : "Specific YLL data for ..head and neck cancers are not available. ....Brain tumour patients suffer more than three times the mean loss of life with an AYLL figure of just over 20 years.....Tumours of the brain and CNS have the highest AYLL of all 17 tumour sites, but a rather modest 1.5% of NCRI research spending"
- Time is not on the side of patients with high grade or newly diagnosed brain tumours as their prognosis is so poor

Section 4 : Evidence and interpretation

- **4.1.4 and 4.1.10** The long term survival data is significant - it shows a 40.6% improvement at 12 months survival for radiotherapy plus temozolomide over the radiotherapy only group.
- **4.1.11** Subgroup analysis (MGMT) is mentioned and although MGMT is likely to be a predictor of benefit from temozolomide, this trial is ongoing and not yet validated. It is amazing that this unproven data was

considered and yet the completed data of subgroup analysis appears not to have been taken into consideration in the final analysis of the ACD

- **4.1.12** ACD highlights that greater benefit was observed with temozolomide in the subgroup of patients who had complete resection. Median survival was 14.2 months in the radiotherapy only group and 18.3 months in the radiotherapy plus temozolomide group. This represents a survival advantage of 4.1 months which to a terminally ill patient and their family amounts to a significant difference. Why did the Assessment Group not conduct an analysis to assess the cost-effectiveness of temozolomide in this patient group?

- **4.3.1** Although the Committee state that they have considered the clinical evidence and comments provided by patient groups, it appears that they have based their decision purely on the AG economic model. The AG model acknowledge that their model is sensitive to certain data and the assumptions they have used. As the economic model used appears pivotal to the success or failure of this assessment, it would be helpful to know whether the model had been properly validated and if so by whom and how? Is such a QALY dominated model appropriate for an extremely aggressive disease such as GBM?

- **4.3.2** The ACD states that "the quality of life of patients is paramount at all stages of the disease.." yet although available evidence suggests that temozolomide/carmustine implants do not have a detrimental effect on quality of life, this appears to have been discounted.

- **4.3.4** The concerns expressed with regard to access to radiotherapy in some situations should not be used as an argument not to recommend temozolomide/carmustine. Expert clinicians would not treat with temozolomide or carmustine if radiotherapy was not available, as in their professional capacity they would realise that this would be a waste of resources.

- **4.3.5** This point is impossible to understand and needs clarification.

- **4.3.9** QALY analysis may not be appropriate for this disease. The quality of life data was assessed in the temozolomide trial using a disease specific instrument. There is no validated methodology for measuring utilities based on this instrument. In the light of this, cost utility analysis was not feasible.

- **4.3.13** Sub group analysis for temozolomide has been ignored. Fully and partially resected patients along with fitter patients all benefit.

Section 5 : Proposed recommendations for further research

- It should be noted that USA and Europe currently use these treatments as the standard care based on trials conducted up to now.

- Trials involving the UK are already ongoing (eg temozolomide MGMT). If these treatments are not recommended, the UK would have to withdraw from the trials (this would include the current Edinburgh study). Undoubtedly the UK will drop behind the rest of the world in its treatment of glioma patients if these products are not recommended for use in the UK. (What a tragedy that a UK generated drug such as temozolomide should be used across the world but denied in the UK!)

- The ACD preliminary recommendation is for restricted use to well-designed RCTs. However this means that the 1,800 (approx) patients diagnosed with high grade glioma per year in the UK would largely be denied treatment that top experts/clinicians in the UK consider to be of benefit. The emotional and psychological suffering endured by high grade glioma patients (and their families/carers) is huge. The knowledge that such patients are being denied effective treatment can only lead to an increase in stress levels for those concerned and have an adverse effect on the last months of their lives.

Section 9 : Proposed date for review of guidance

- The Samantha Dickson Research Trust sincerely hope that the committee's recommendations will receive further consideration and that the immediate outcome will mean access to the use of carmustine implants and temozolomide for newly diagnosed and high grade glioma patients. Any postponement for review in August 2009 will cause enormous frustration and suffering to such patients and their families/carers. It is bewildering that an NHS willing to prescribe methadone for drug addicts and patches for smokers will openly deny access to effective treatments for seriously ill patients who would give anything to have a few more months to live.

- The ACD calls into question the willingness of brain tumour charities (and members of the British public) to continue to raise funds for research if progress in the field of brain tumour research is met with such barriers.