Comments on NICE Evaluation Report on Carmustine Implants and Temozolomide

General comments.
These guidelines will cause considerable disquiet in the neuro-oncology community since they suggest that the NHS in England and Wales is not able to offer effective new treatments for high grade glioma, which are widely used elsewhere and have recently been approved for NHS funding in Scotland. Temozolomide and external beam RT are considered standard approach for GBM across the world and this has already become the standard treatment arm in international studies. This will make it difficult to convince well informed patients that they should not travel elsewhere for treatment and/or seek treatment in the private sector.

It is also likely to become difficult to accrue to studies with RT only as a treatment arm. The assumption that studies involving these agents will be able to produce useful additional information is likely to prove incorrect. The involved pharmaceutical companies are very unlikely to support such studies and patients will not wish to take part in them.

Specific comments on ACD report

4.2 The main conclusions are based on a novel health economic analysis which has never been validated. No separate analysis has been carried out to assess benefit in good prognosis subgroups. These have been well defined by the RCT of Temozolomide and RT and it is these patients who are likely to gain most from adjuvant treatment.

4.2.10 Assumptions on the effect of Temozolomide on long term survivorship are limited by follow up in largest study. This should be re-evaluated when longer follow up data are available, this will be before the 2009 re-evaluation date suggested in the document.

4.3.3 The suggestion that other chemotherapies may be as effective in this setting is supposition. Mechanisms of action/interaction with RT are likely to be different and, particularly with PCV bone marrow toxicity is more likely.

4.3.4 Longer survival in the control arm in the EORTC study is likely to be due to increased proportion undergoing more radical surgery and early radiotherapy. This is a separate issue and may be used as an argument to improve surgical management and timing of RT rather than not give adjuvant chemotherapy. Use of concomitant regime within a specified time frame after surgery could be an effective driver to improve RT waiting times in this patient group.

4.3.13 The assumption that MGMT status will be a strong predictive indicator of response is based on a single study in which only 50% of tumours could be assessed and should not be used as an argument against treating the whole GBM population until these data are validated in additional studies.

Specific comments on Evaluation Report

i. Subgroup analysis for patients with better performance status is available (supplementary material to Stupp NEJM paper). This should be used in health economic analysis, section 5.7.2.3

ii. The health economic model used makes significant assumptions about survivorship and QOL in 2 year survivors after Temozolomide. These are not supported by available data, which are too immature to address this.

iii. There are now data describing the effects of adjuvant Temozolomide on QOL during treatment (Taphoorn et al Lancet Oncol Nov 17 2005). This suggests that it would be unusual for adverse effects of Temozolomide to affect cost per QALY.