ABSTRACT

Background

High grade glioma (HGG) is an aggressive form of brain tumour the treatment of which usually entails biopsy or resection where possible followed by radiotherapy. Temozolomide is a novel oral chemotherapeutic drug that penetrates into the brain and has a low incidence of adverse effects.

Objectives

To assess whether temozolomide holds any advantage over conventional therapy for HGG in either primary or recurrent disease settings.

Search strategy

The following databases were searched: the Cochrane Central Register of Controlled Trials (CENTRAL) Issue 2, 2007. Medline, EMBASE, Science Citation Index, Physician Data Query and the Meta-Register of Controlled Trials. Reference lists of identified studies were searched. The Journal of Neuro-Oncology was hand searched from 1999 to 2007 including conference abstracts. Neuro-oncologists were contacted regarding ongoing and unpublished trials.

Selection criteria

Randomised controlled trials (RCTs). Interventions included the use of temozolomide during primary therapy or for recurrent disease. Patients included those of all ages with a proven pathological diagnosis of HGG.

Data collection and analysis

Quality assessment and data extraction were undertaken by two review authors. Outcome measures included survival, time to progression, quality of life (QOL) and adverse events.

Main results

In primary disease two RCTs were identified, enrolling a total of 703 patients, that investigated concomitant and adjuvant temozolomide in Glioblastoma Multiforme (GBM). Temozolomide increased survival (hazard ratio (HR) 0.84, confidence interval (CI) 0.50 to 0.68, p < 0.001) and an increase in time to progression (HR 0.52 CI 0.42 to 0.64 p < 0.0001). This was without having a statistically significant negative effect on QOL and with a low incidence of early adverse events. Grade 3/4 haematological toxicity was found in 5 to 14%. The long term effects of temozolomide are still to be assessed. In recurrent GBM a single trial enrolling 225 patients in total
found that temozolomide did not increase overall survival but it did increase time to progression (HR 0.68 CI 0.51 to 0.90 p0.008). Severe adverse events were low in this setting.

Authors’ conclusions

Temozolomide is an effective therapy in GBM for prolonging survival and delaying progression as part of primary therapy without impacting on QoL and with a low incidence of early adverse events. The frequency and severity of late adverse events is unknown. In recurrent GBM it improves time to progression but not overall survival. These findings are from three good quality but non-blinded RCTs of over 900 patients in total.
**PLAIN LANGUAGE SUMMARY**

High grade glioma is a rapidly progressive form of brain tumour: half of all patients will die within a year of diagnosis even after treatment with surgery and radiotherapy.

High grade glioma (HGG) is a rapidly progressive form of brain tumour with a poor survival rate even after treatment with surgery and radiotherapy. We found two trials, enrolling 703 patients in total with a newly diagnosed glioblastoma multiforme (a form of HGG), that studied chemotherapy with temozolomide during and after radiotherapy. This was compared with radiotherapy only. Those who received temozolomide had an improved survival and delayed time to recurrence. The short term adverse events associated with temozolomide are low but can be severe, while the long term effects are unknown. In recurrent disease a single trial was identified that included 225 patients with glioblastoma multiforme at first relapse. In this instance temozolomide delayed progression but did not improve overall survival. No RCTs investigated the use of temozolomide in HGGs other than glioblastoma multiforme. All these trials enrolled highly selected patients with good prognostic features that are not entirely representative of all patients with glioblastoma multiforme limiting the general applicability of these results.