Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion in NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Temozolomide (TEM), a chemotherapy option used for malignant gliomas, was studied. TEM was administered at a dose of 150 mg/m2 per day orally for 5 days every 28 days. The dose could be increased to 200 mg/m2 if no prior chemotherapy had been administered or on the second cycle if no significant haematological or other toxicity was noted.

Type of intervention
Treatment and palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with a diagnosis of malignant glioma. Patients were excluded if they had a diagnosis other than those malignant brain tumours in which TEM treatment was indicated in accordance with the British Columbia Cancer Agency (BCCA) TEM chemotherapy protocol. They were also excluded if they had received LOM as part of a multi-drug chemotherapy regimen, had received LOM or TEM as adjuvant therapy rather than for recurrent disease, and if they had previously relapsed. Also excluded were patients who had received a second chemotherapy agent within 6 months of the initial prescription for TEM or LOM.

Setting
The setting was a hospital. The economic study was carried out in British Columbia, Canada.

Dates to which data relate
The clinical and economic data were gathered from November 2001 to October 2003. The price year was unclear.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the clinical analysis.

Study sample
Power calculations were not reported. Patients were eligible if they were registered as cancer patients with a diagnosis of malignant glioma, and had filled a prescription in British Columbia for single-agent LOM between 1 November 2001...
and 31 October 2002 or for single-agent TEM between 1 November 2002 and 31 October 2003. Of the 188 patients initially identified, the application of exclusion criteria left a final study sample of 50 patients (60% men) in the TEM group and 28 patients (75% men) in the LOM group. The median age of the patients was 54 years (age range: 22 - 80) in the TEM group and 53 years (age range: 26 - 78) in the LOM group.

**Study design**
The clinical evidence came from a retrospective review of patient charts, which was carried out at several medical centres. Data came from the Cancer Agency Information System and the Cancer Registry. The planned length of follow-up was 6 months. No patient was lost to the follow-up assessment. The outcome assessment was not performed blind.

**Analysis of effectiveness**
All of the patients included in the initial study sample appear to have been included in the analysis of effectiveness. The primary outcome measure was 6-month progression-free survival (PFS). The outcome of 6-month PFS was a dichotomous outcome based on patients vital status at 6-months post-initiation of therapy; either alive with no disease progression or deceased/disease progression based on progress notes of clinical or radiological progression. The secondary outcomes included overall survival (OS) and 6-month OS. OS was calculated using the Kaplan-Meier method. The study groups were comparable at baseline in terms of their demographic characteristics. However, patients who received TEM differed significantly from those who received LOM in three areas. More specifically, receipt of prior chemotherapy, receipt of chemotherapy after receiving the study treatment, and the mean duration of follow-up.

**Effectiveness results**
The rate of 6-month PFS was 52% (95% confidence interval, CI: 37.6 - 66.1) with TEM and 42.9% (95% CI: 25 - 62.6) with LOM, (p=0.438).

The rate of 6-month OS was 72% (95% CI: 57.3 - 83.3) with TEM and 64.3% (95% CI: 44.1 - 80.7) with LOM, (p=0.479).

The median OS was 40.9 weeks (95% CI: 27.7 - 54) with TEM and 46.7 weeks (95% CI: 19.5 - 73.9) with LOM, (p=0.896).

**Clinical conclusions**
The effectiveness analysis showed that the two chemotherapy options were equivalent.

**Measure of benefits used in the economic analysis**
The summary benefit measures used in the economic analysis were median OS and 6-month PFS. These were derived directly from the clinical study.

**Direct costs**
The cost analysis was carried out from the perspective of the BCCA. The economic evaluation considered the costs of the drugs (LOM and TEM), labour and supply. The unit costs were not presented separately from the quantities of resources used. The resource use data came from a review of the charts of patients included in the effectiveness study. The costs were estimated using a previously used costing template. Discounting was not relevant since the costs were incurred during one year. The price year was not reported. Since the number of cycles of chemotherapy differed between the groups, the costs were presented per cycle and then grouped as total costs.

**Statistical analysis of costs**
The costs were treated deterministically.
Indirect Costs
The indirect costs were not included in the economic evaluation.

Currency
Canadian dollars (Can$).

Sensitivity analysis
A univariate sensitivity analysis was carried out to examine the robustness of the cost-effectiveness ratios to variations in the two benefit measures. The benefit measures were varied within their 95% CIs.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The median number of cycles per patient was 6 (range: 1 - 22) with TEM and 4 (range: 1 - 7) with LOM.

The median cost per patient was Can$11,660 (range: 1,808 - 44,584) with TEM and Can$189 (range: 37 - 429) with LOM.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio was calculated to combine the costs and benefits of the two chemotherapy regimens.

When median OS was used as the summary benefit measure, TEM was dominated by LOM, which was both more effective and less costly.

When median 6-month PFS was used as the summary benefit measure, the incremental cost per each additional per cent of patients progression free with TEM over LOM was Can$1,261.

The sensitivity analysis showed that when median OS was varied, LOM remained the dominant strategy except at the low ends of its 95% CI. When median OS was prolonged with TEM, as compared with LOM, the cost per additional week of survival gained ranged from Can$332 to Can$/1,571. When changing the 6-month PFS, the TEM results remained robust until the high end of the 95% CI for LOM.

Authors’ conclusions
Temozolomide (TEM) was not a cost-effective chemotherapy option for patients with malignant gliomas in Canada. TEM did not offer improved survival in comparison with lomustine (LOM), which was cheaper.

CRD COMMENTARY - Selection of comparators
The selection of LOM as the basic comparator was appropriate as the authors stated that it reflected the protocol treatment for patients with malignant gliomas in British Columbia. It was also stated that LOM was the predecessor of TEM. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The clinical data were estimated from a retrospective review of a medical database. The use of administrative data is usually associated with several limitations, which might have introduced confounding factors and assessment bias. Further, outcomes of interest must be extracted within the administrative restrictions of the database. The authors noted
that, owing to sequential timeframes of data collection, the number of censored cases in each of the two groups was discordant. In addition, the use of very strict exclusion criteria (required to limit potential bias) meant that two small groups of patients, which were not well balanced at baseline, were considered. In fact, the study was underpowered to detect statistically significant differences between the groups. However, the authors noted that the validity of their results was enhanced not only by the overlapping between CIs, but also by the similar results observed in the literature.

Validity of estimate of measure of benefit
The summary benefit measures were specific to the disease considered in the study and were derived directly from the clinical study. However, the use of OS is quite comparable with the benefits of other health care interventions for patients with cancer. The authors stated that some benefits of care, mainly those with an impact on quality of life, were not taken into consideration and this might have resulted in an underestimation of the benefits of TEM.

Validity of estimate of costs
A limited perspective was adopted in the cost analysis. The authors noted that other categories of direct medical costs, such as the costs of supportive care, were not relevant and were not considered in the analysis, although their inclusion would have been interesting. The unit costs were not reported separately from the quantities of resources but the costs were presented per cycle, which might help replication of the results in other settings. Limited information on the source of the costs was provided. Further, the cost estimates were specific to the authors’ setting. The price year was not explicitly reported, which limits the possibility of performing reflation exercises in other time periods.

Other issues
The authors made extensive and detailed comparisons of their clinical findings with those from other studies. The number of patients, demographics, baseline clinical characteristics, and clinical end points of three published studies were reported and compared with those observed in the current study. The authors concluded that consistent results were observed, which supported the validity of their estimates. The issue of the generalisability of the study results to other settings was not explicitly addressed and a limited sensitivity analysis was carried out. Thus, the external validity of the analysis was low. The study referred to patients with malignant gliomas and this was reflected in the authors’ conclusions.

Implications of the study
The study results suggested that when only survival outcomes and direct costs are considered, TEM is not a cost-effective chemotherapy agent for patients with malignant gliomas.

Source of funding
None stated.

Bibliographic details

Other publications of related interest


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Subject indexing assigned by CRD

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