MST was 30.3 weeks with 64% (CI = 51–81%) of patients surviving at 6 months (ST-6) and 28.6% (CI = 16–49%) at 12 months (ST-12).

Conclusion: TMZ as a second line regimen is a valid option in patients with heavily pretreated GBM.

1278 POSTER

Temozolamide (TMZ) in second-line treatment after pcv In glioblastoma multiforme (GBM). Experience from a single Portuguese Institution

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Purpose: Temozolamide is a new cytotoxic alkylant agent which has recently been aproved in Portugal for the treatment of recurrent high-grade glioma. A retrospective study was performed to assess the survival (Kaplan-Meier) of patients treated with TMZ at the time of relapse.

Methods: From September 1999 to March 2001, 16 patients with recurrent GBM who had prior PCV chemotherapy, were given TMZ 150-200mg/m2/day during 5 days every 28 day cycle.

Results: To date 16 patients with a medium age of 58 (ranges: 31-74) and a median KPS of 80% have been enrolled. The estimated one-year survival is 16%. The median overall survival was 6,5 months.

Conclusions: Despite the small scale of the sample, the overall survival achieved with TMZ is similar to other reports. These promising data suggest that randomized trials should be undertaken to assess its use in first-line therapy, its inclusion in combination chemotherapy regimes and its effectiveness with concurrent radiotherapy.

1279 POSTER

Phase I study with continuous infusion (CIV) dose escalated 5 day schedule topotecan (TPT) and radiation therapy (RT) for patients with previously untreated glioblastoma (GBM)

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Rationale: TPT has been shown to have (1) good penetration across the blood brain barrier in non-human primates (Sung Cancer Res 1994; 54: 5118), (2) significant anti-tumor activity against human brain tumor xenografts (Polina, J. Neurooncol 1998; 39:217) and (3) synergy with RT in humain glioma cell lines (J P Lamond J Neuroonco,1996; 30:1). The dose/schedule of topotecan chosen would be of value.

Objective: A phase I study was performed to determine the dose-limiting toxicity (DLT) and maximun tolerated dose (MTD) of CIV TPT in combination with RT in patients with GBM.

Methods: After surgery or stereotactic biopsy, patients received (1) RT using 2 Gy/fraction, 5 times/week with total dose of 60Gy reached in 6 weeks and (2) TPT with doses escalated from 0,6 to 1,0 mg/m2/d as CIV from day 1 to day 5 on week 1,3 and 5 during RT. DLT was defined as febrile neutropenia, grade 4 neutropenia more than 7 days, grade 4 thrombocytopenia, thrombocytopenia requiring platelets transfusion or any grade 3 toxicity except alopecia, nausea and vomiting. All patients had anticonvulsivant prophylaxis with valproic acid.

Results: 20 patients have been enrolled in the protocol between January and April 2001

DLT is hematologic with no other grade 3 or 4 treatment related toxicity except one confusion in one patient. MTD is 1,0 mg/m2/d and an intermediate level at 0,9 mg/m2/d is ongoing to determine the recommended dose. The table summarizes DLT according to TPT level and number of patients:

TPT Dose mg/m2	N	DLT	Type of toxicity
0,6	3	0/3	None
0,8	6	1/3	Thrombocytopenia gr 4 (1)
0,9	5	Ongoing	Not yet known
1,0	6	4/6	Thrombocytopenia gr 4 (3), platelet

Conclusion: The MTD of CIV TPT in association with RT in patients with GBM is 1,0 mg/m2/d, The DLT is hematologic. 0,9 mg/m2/d appears to be the appropriate phase II dose, but needs to be confirmed.

1280 POSTER

A phase II study evaluating the efficacy and safety of temozolamide (tmz) post and concurrently with radiotherapy (RT) in the treatment of patients with previously untreated high grade gliomas

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Purpose: It is known that the prognosis of patients with high grade gliomas is dismal. It is slightly improved by the use of RT. The addition of TMZ, as a new chemotherapeutic agent in the treatment of these patients, is studied.

Methods: Since November 1997, we have studied 31 patients suffered from high grade gliomas.Eligible histologies include glioblastoma multiforme (28 patients) and anaplastic astrocytoma (3 patients). All patients received RT at a total dose of 60-64 Gy, 2 Gy per fraction, within 6-6.5 weeks and they hadn't received prior chemotherapy. In group I (14 patients) TMZ was prescribed 3 weeks after the completion of RT at a dose of 200 mg/m2/day for 5 consecutive days. In group II (17 patients) TMZ was administered concurrently with RT at a dose of 150 mg/m2/day for 5 concecutive days. At the end of RT patients received 2 cycles of TMZ. We continued with TMZ at a dose of 200 mg/m2/day, every 28 days. The dimensions of the lesions were evaluated 3 times during the study with MRI, at the beginning of RT, after 3 and 6 cycles of TMZ.

Results: In group I, patients had a median age of 54 years (ranged from 27 to 73 years) and in group II, patients had a median age of 58 years (from 26 to 83 years). At the time of enrollment in the study, all patients had Karnofsky Performance Status (KPS) greater than or equal to 70. In group I 10 patients and in group II 7 patients had undergone surgery before RT, the rest had undergone stereotactic biopsy. Adverse events were nausea and vomiting (55%), fatigue (40%), constipation (45%). Hematological undesirable consequenses included leukopenia (4/14, 5/17), thrombocytopenia (7/14, 11/17), anemia (2/14, 3/17). Many patients had high prices of serum liver enzymes (AST, -GT). Two patients (1/14, 1/17) discontinued treatment because of adverse events related to TMZ. During the study, 16 patients (8/14, 8/17) were died after a mean survival of 11 months in group I, and of 9 months in group II. Fifteen patients (6/14, 9/17) are still alive with a mean survival of 18 months in group I, and of 7 months in group II. In group I, the mean PFS was 12.5 months and in group II 7 months.

Conclusions: According to our study, it seems evidently that the administration of TMZ at a dose of 200 mg/m2/day after the completion of RT is more effective in terms of PFS and overall survival. The KPS of the patients was satisfactory during the study and TMZ showed a good toxicity profile and desirable antitumour activity.

1281 POSTER

Gemistocytic astrocytoma – Astrocytoma II with unfovorable prognosis

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Three major histopatological variants of diffusely infiltrating astrocytomas are recognised: fibrillary (FA), protoplasmatic (PA) and gemistocytic. They are designed in WHO classification of tumours as grade II. Gemistocytic Astrocytoma (GA), the second most common variant account for no more 20% of astrocytoma. GA often behave more aggressively than other types of diffusely infiltrating Astrocytomas, and around 80% of these tumours progress to GBM. Surprisingly, the vast majority of gemistocytes are in a nonproliferative state, which suggest terminal differentiation. However GA contain highly variable small glial cell component which appears be mitotically active. P53 mutations are a genetic hallmark of GA, whereas the incidence of p53 mutations in astrocytomas of other variants is low.

Material: In the years 1983 - 98 in our Hospital there were treated 462 adults with Astrocytomas I–IV. In 34 pts were diagnosed GA in 20 and Anaplastic GA in 14. There were 25 men and 9 women; the median age was 44.9. Tumours in the temporal lobe were most often. All pts were undergone surgery procedure following by radiotherapy (60 Gy for the tumour bed). Chemotherapy (PCV) was done for 13 pts with the tumour test after operation.

Results: Material was analysed according to following tests Cox, Cox-Mantel, log-rank, Wilcoxon Peto Peto. The median recurrence time free was 14 m. 25% of pts died in the 37 m after operation, 50% pts survived 77 m, and 25% live out more than 95 m.