diameter on axial plane images. Crude LC rate was 81% (25/31). Six patients failed locally, 2-3 months after FSRT(median 9). Actuarial 1-year LC rate was 74%. Median survival time was 351 days, with actuarial overall survival rate at 12 and 18 months of 48% and 14% respectively. Thirty-eight percent of patients (11/29) developed new metastases outside the treatment volume after 2-24 months (median 11)and 4 received whole-brain irradiation as salvage treatment. In the majority of patients (10/29) the cause of death was systemic tumor progression. All treatments were well tolerated and no acute complications were seen, with the exception of transient headache and limited nausea.

Conclusion: This retrospective study suggests that FSRT with few fractions and a short treatment period is a tolerable and effective form of intensive local treatment of brain metastases.

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Three different fractionation schemes in glioblastoma multiforme: a single center experience with 430 patients

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Purpose: To evaluate the role of fractionation in the management of newly diagnosed glioblastoma multiforme (GBM).

Patients and methods: From January 1980 to June 2000, 430 consecutive patients with histologically confirmed GBM were treated at our institution. Median age was 59 years (19-81), Karnofsky Performance Status >/= 70 in 290 patients. 86 patients had a biopsy, 344 underwent resection. Primary radiotherapy was given in conventional fractionation - 5 x 2.0 Gy, total dose 60.0 Gy (n = 97). Postoperative radiotherapy was given hypofractionated - 5 x 3.5 Gy, total dose 42.0 Gy - (January 1980 - July 1983; n = 104) or hyperfractionated - 5 x 3 x 1.5 Gy, total dose 54.0 Gy (August 1983 - June 2000; n = 229). Survival probabilities were computed using the method of Kaplan-Meier.

Results: Median actuarial survival probabilities were as follows: All patients 8.6 months; biopsy 5.9 months vs. resection 9.0 months (p = 0.03); hypofractionation 8.2 months vs. hyperfractionation 9.05 months vs. conventional fractionation 8.5 months (p = 0.56). In a proportional hazards model, independent variables indicating a better prognosis were younger age (< 59 years vs. >/= 59 years: RR 0.84, 95%-CI 0.76-0.93), good performance status (KPS >/= 70 vs. KPS < 70: RR 0.83, 95%-CI 0.75-0.92), normal LDH level (LDH < 240 vs. LDH >/= 240: RR 0.77, 95%-CI 0.67-0.89) and total dose (RR 0.98/extra Gy, 95%-CI 0.97-0.99).

Conclusions: In this pure GBM series fractionation did not affect survival. Shortening treatment time by modifying fractionation does not compromise life expectancy. Besides the validation of known prognostic factors like age, KPS and total dose we found elevated LDH levels to have a strong negative influence on survival.

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Temozolamide in previously treated high-grade gliomas patients

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Objectives: To assess the efficacy and toxicity of temozolamide in high grade glioma patients previously treated.

Patients and Methods: Histologically proven high grade glioma patients (pts) with measurable disease were included. Temozolamide was administered at a dose of 150 mg/sqm five consecutive days every four weeks. If no grade III or IV toxicity appeared dose could be increases up to 200 mg/sqm. Response was assessed every 3 courses according to McDonald's criteria and therapy maintained until progression or unacceptable toxicity.

Results: 49 patients have been included, 33 (67%) males, median age 48 (22-69), ECOG performance status 0/1/2 in 5/23/21 pts. Median tumour area was 13.5 cm2 (1-63) Previous chemotherapy lines 0/1/2/3 in 4/36/5/3 pts, with a median of 4 chemotherapy courses per patient (0-8). All except 1 had received radiotherapy. Histology was glioblastoma 30, anaplastic astrocytoma 14, oligodendroglioma 2, and oligoastrocytoma 3.

Overall response rate was 22:4%, with complete response (CR) in 4 patients (8.2%, 2 patients with oligoastrocytoma and 2 with anaplastic astrocytoma), and partial response (PR) in 14.3% (7 pts). stable disease (SD) was achieved in 22.4%. Response according to histology was glioblastoma 10% PR (3), 33% SD (10), overall response 10% anaplastic astrocytoma 14.3% CR (2), 21.4% PR (3), 64.3% progressive disease (PD) (9), overall response 60% and oligodendroglioma or oligoastrocytoma 40% CR (2), 20% PR (1), 20% SD and 20% PD, overall response (60%). Actuarial median survival of all patients was 36 weeks (CI95% 27-44). glioblastoma 29 weeks (CI95% 12-45), anaplastic astrocytoma 46 weeks (CI95% 3.5-88), median survival is not reached for oligodendroglial tumours with a median follow up of 88 weeks (21-197).

No grade III or IV toxicity has been reported, and main toxicity were mild thrombocytopenia and moderate nausea easily controlled with 5-HT3 antagonists.

Conclusions: Temozolamide is active in high-grade glioma patients, even if previously chemotherapy treated. Anaplastic astrocytoma and oligodendroglial tumours appear to have better response and survival. This treatment is well tolerated with minimal toxicity

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Expression of PDGF-R, DCC, MDM2 and P16 in human gliomas

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Gliomas constitute a group of very aggressive and almost incurable primary brain tumors. Changes in the expression of the oncogenes PDGF-R and MDM2 and that of the suppressors DCC and p16, have been associated to tumor progression. In this work we studied, by immunohistochemistry, the expression of the aforementioned molecules in 41 gliomas of different histological grade of malignancy [low grade (LGA), anaplastic astrocytoma (AA) and glioblastoma multiform (GBM)]. A high expression of PDGF-R (>50% of positive cells) was found associated with the histological grade (40% of GBM vs. 15% LGA and AA tumors, NS). Only a few cases presented overexpression of the oncogene MDM2, with no differences among the three groups of gliomas, and the expression of DCC was lost in only 11% of the GBM. On the other hand, found a significant association between the loss of expression of the suppressor p16 and the histological grade (LGA: 0%, AA: 12% and GB 26%, p<0.05). This correlation was not modified when variables such as sex, age and Karnofsky status were introduced in the analysis. Among all the molecules analyzed, only p16 staining showed a significant correlation with overall survival. While 78% of the patients with the longest survival (>1 year) expressed p16, only 22% of those who were alive for less than one year after diagnosis did (p<0.05). In conclusion, the association between the loss of the cell cycle inhibitor p16 expresssion in human gliomas and the histological grade was independent of the other prognostic variables studied. Moreover, this lack of expression showed a correlation with a shorter overall survival.

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Temozolomide as a second line regimen after BCNU and procarbazine in recurrent glioblastoma multiforme: A phase II study

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Purpose: To investigate the efficacy of temozolomide (TMZ) in relation to response rate, toxicity, and progression free survival at six months (PFS-6), a phase II study was conducted in patients with recurrent glioblastoma multiforme (GBM) following surgery plus radiotherapy and a first-line regimen based on nitrosourea, procarbazine and vincristine.

Patients and Methods: 42 patients with GBM, of which 8 (19%) were previously low grade astrocytoma or oligodendroglioma, were administered TMZ at the dose of 150 mg/m^2/daily for five days every 4 weeks.

Results: The response was assessed in all 42 patients: we observed 2 complete responses (CR) (4.7%), 6 partial responses (PR) (14.3%), and 9 stable disease (SD) (21.4%), with CR + PR = 19% (95% Confidence Interval [CI] = 7–31%). The median TTP for all 42 patients was 11.7 weeks, (CI = 9–22%) while progression free survival at 6 months (PFS-6) and at 12 months (PFS-12) was 24% (CI = 14–42%) and 8% (CI = 2–27), respectively.