to compare the efficacy and safety of TMZ administered concomitantly and sequentially to RT versus RT alone in patients with newly diagnosed GBM.

Material and methods: Between January 2000 and December 2002, 110 patients with pathologically confirmed newly diagnosed GBM were randomized to receive either TMZ 75mg/m^2/daily orally, concomitantly with RT (60 Gy in 30 fractions, Group A: n=57), followed by 6 cycles of TMZ (150mg/m^2, days 1-5 and 15-19 every 28 days) or RT alone (60 Gy in 30 fractions, Group B: n=53). The patients characteristics are comparable for both treatment groups.

Results: Median time to progression (TTP) was significantly higher in Group A (13.3 months) compared to Group B (7.6 months) (p=0.015). Progression free survival (PFS) at 1 year: Group A: 58%, Group B: 17%. Overall survival (OS) was also significantly better in the combined modality group: 1year OS: 55% vs 16%; 2years OS: 15% vs 0% (p=0.0001). Toxicity was mainly haematological; in the TMZ+RT Group Grade 3 leukopenia in 2 pts and Grade 3 thrombocytopenia in 3 pts was observed. One patient experienced Grade 4 neutropenia, thrombocytopenia and sepsis leading to death. 2 patients discontinued therapy because of myelosuppression. The other side effects were mild: rash (3 pts), constipation (1 pt), arthralgies (1 pt). In the RT alone Group was observed Grade 3 thrombocytopenia in 1 patient.

Conclusions: TMZ combined with RT (concomitantly and sequentially) appears to be more effective than RT alone in patients with newly diagnosed GBM. The combined modality treatment was well tolerated in our patients.

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Combined treatment with Radiotherapy and Temozolomide in recursive partitioning analysis (RPA) class V-VI glioblastoma patients. Preliminary results of a multicenter prospective study.

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Background: To determine feasibility, toxicity, and efficacy of a new combined curative treatment with Temozolomide (TMZ) and Radiotherapy (RT) in patients with poor prognosis, pathologically proved, glioblastoma multiforme.

Patients and Methods: Patients with histological diagnosis of glioblastoma multiforme, submitted to biopsy only or partial resection, age > 49 years, Karnofsky Performance Status > 50, (RPA class V-VI) were prospectively treated with curative RT (60Gy in 30 fractions of 2Gy for 5 days a week) and full dose of TMZ (200mg/m^2 for 5 days) administered during RT (the first day of the forth week of irradiation, at the time of the 16th dose of RT), followed by TMZ (200mg/m^2 for 5 days) every 28 days for six courses. Toxicity was recorded using the Common toxicity criteria version 2.0 and the overall survival was calculated from the time of surgical procedure (biopsy or resection with macroscopic residual disease).

Results: From March 2002 to January 2003 were enrolled 20 patients (3 female and 17 male) with a median age of 61.5 years (range 51-72). A total of 82 courses of TMZ were administered (median 4, range 1-7) and all patients completed the planned RT at 60Gy. The most common toxicity was hair loss in the treatment area (20/20 patients); a grade 2 neutropenia was observed in 3/20, grade 2 thrombocytopenia in 2/20, grade 2 vomiting in 1/17, and grade 1-2 nausea in 4/20. At the last follow-up (15/03/2002), 14 patients are alive with survival ranging from 2 to 12.5 months. Six patients died respectively at 2, 2, 2.5, 5, 6, and 7 months.

Conclusions: these very preliminary data seem to demonstrate that a combined curative treatment with RT and TMZ is feasible with low-moderate toxicity in poor prognosis glioblastoma patients. The study is ongoing.

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Incidence and severity of anaemia in patients with primary lymphoma of the central nervous system treated with high-dose methotrexate

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Background: Only little data is available on anaemia in patients (pts) with non-Hodgkin's lymphoma (NHL). In pts with extracerebral NHL treated with polychemotherapy, anaemia grade 1 (haemoglobin [Hb] 9.5-10.9 g/dL) or 2 (Hb 8.0-9.4 g/dL) according to the World Health Organization (WHO) classification was observed in about 28% and WHO grade 3 (Hb 6.5-7.9 g/dL) in about 10% of pts. We evaluated the incidence and severity of anaemia in pts with primary central nervous system lymphoma (PCNSL) before and during treatment.

Material and methods: 121 pts (62 male, 59 female, median age 62 years [range 22-83 years]) with newly diagnosed PCNSL received a total of 437 cycles high-dose methotrexate (HD MTX, 4 g/m^2 body surface area per cycle, repeated every 2 weeks up to a maximum of 6 cycles).

Results: Only 4 of 45 evaluable pts (8.9%) had mild (WHO grade 1) anaemia before chemotherapy. During HD MTX, anaemia (Hb d 10.9 g/dL) was seen in 61 pts (50.4%). Anaemia WHO grade 1 and 2 was observed in 24 pts (19.8%) each. The highest grade seen when considering all HD MTX-treated pts was anaemia WHO grade 3. It was observed in 13 pts (10.7%). Regarding the HD MTX cycles received, anaemia WHO grade 1 and 2 occurred in 137 cycles (31.4%), and anaemia WHO grade 3 was observed in 14 (3.2%) cycles. 286 cycles (65.4%) of HD MTX were not associated with anaemia.

Conclusions: We conclude that in contrast to pts with extracerebral NHL, PCNSL pts are rarely anaemic at the time of diagnosis, and significant anaemia often only develops during HD MTX therapy. The incidence of anaemia WHO grade 1 and 2 in PCNSL pts treated with HD MTX seems to be higher, and severe anaemia (WHO grade 3) at least equally frequent compared to pts with extracerebral NHL treated with polychemotherapy. Anaemia may mimic neurological symptoms related to PCNSL and may therefore even influence therapeutic intervention and outcome. Moreover, a positive correlation between Hb levels and quality of life in pts with haematological malignancies has been reported. Additionally, anaemia was found to be an independent prognostic factor in NHL patients. Therefore, like pts with extracerebral NHL, PCNSL pts treated with HD MTX should be carefully watched for signs and symptoms of anaemia, and, if indicated, be given blood transfusions and/or erythropoietin according to international guidelines. First data of our pts treated with erythropoietin shows an adequate Hb response. Updated results will be presented.

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Partial brain irradiation (PBI) or whole brain irradiation (WBI), the justified solution

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Background: Postoperative conventional radiotherapy (RT) improved survival for glioblastoma multiforme (GBM) and astrocytoma anaplasticum (AA), but local recurrences were stile a reason of pore outcome. The main purpose of this study was to compare response in patients (pts) with malignant astrocytoma treated by PBI and WBI. Also, an evaluation was made to the acute radiation toxicity.

Materials and methods: Between 1998-2000, 70 pts with supratentorial malignanat astrocytomas treated at the Institute of Radiotherapy and Oncology in Skopje were enrolled in study. Pts were randomized in two groups according the used treatment volume. The treatment volume in the group with PBI covered the contrast-enhancing lesion with 2 sm added margins. They also underwent additional CT scan in the treatment position. In bout groups we applied postoperative conventional RT with 2 Gy daily fractions, to a total dose of 60 Gy. 73% of pts belonged to the group <= 60 years of age, with median age of 40.08 and the rest 27% have a median age of 66.89. Histology consisted of GBM in 77% pts (ratio 3.4:1). Amount of the initial Karnofsky performance status >=80% was 67%.

Results: Objective response (according to WHO criteria) was achieved at 33 (97%) pts with WBI and at 31 (88%) pts with PBI. The overall survival was 12.84 mounts (m), 13.51 m at those with WBI and 12.17 m with PBI. One and two year survival rates at all pts were 31%, 16% respectively. The median disease free survival was 11.8 m, regarding the pts with WBI; it was 11.8 m compared to 10.54 m at the pts with PBI. Median survival at pts with GBM was 8.11 m and at the AA 28.81 m. Favorable prognostic factors on survival according Long-Rank test, were: KPS, histology, age, preoperative duration of symptoms, cortico-therapy during irradiation, the time from the surgery to RT, operation and tumor size. Acute radiation toxicity to brain, ear and skin, evaluated according to RTOG/EORTC score system were more expressed at the pts with WBI.

Conclusions: Although the limitation of the treatment volume does not prolong the duration of survival, its application is justified. Due to rescuing the normal brain tissue PBI leads to a possibility for apply high radiation dozes that could improve the local tumor control.