Landmark analyses were conducted at 9, 18, and 26 weeks using Cox regression models adjusted for important prognostic factors including age, baseline Karnofsky performance score, first vs. second relapse, and treatment arm. The analysis at each time point required that patients survive until the respective landmark. Hazard ratios for survival between the responder and nonresponder groups were calculated. The goodness of fit, robustness, predictive accuracy, and validation of these models were tested.

Results: There was a statistically significant association between OR and survival. Nonresponders were approximately twice as likely to die compared to responders in a given time period.

	9 Weeks		18 Weeks		26 Weeks	
	Resp	NonResp	Resp	NonResp	Resp	NonResp
N	30	127	46	101	51	72
Hazard Ratio (95% CI)	0.52 (0.32, 0.85)		0.48 (0.31, 0.74)		0.43 (0.27, 0.67)	
P Value (Cox model)	0.0091		0.0010		0.0002	

Resp, Responders; NonResp, Nonresponders.

Conclusions: In the BRAIN study, OR rate was clinically compelling when compared to historical controls. This exploratory landmark analysis with pooled treatment arms suggests that patients with an OR had longer residual survival compared with those who did not have an OR. While these conclusions are limited in the absence of a control arm, OR could be considered a potential predictor of survival in this study of BEV-treated patients with relapsed GBM.

8722 POSTER

O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation status is a prognostic factor in anaplastic astrocytomas

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Background: *MGMT* methylation status has been found to be an important prognostic factor in glioblastoma patients (pts). However, further data on the epigenetic feature are needed before its role in rare diseases such as anaplastic astrocytomas (AA) can be established.

Methods: A retrospective analysis was made on a database of 139 AA pts followed prospectively from 01/1995 and 08/2008. We evaluated only pts who met the following inclusion criteria: age $\geqslant$18 years; PS 0−2; histological diagnosis of AA; postoperative radiotherapy (RT) and chemotherapy (CT). *MGMT* status was determined with methylation specific PCR. The study aim was to evaluate the role of *MGMT* methylation status in AA. The log-rank test was employed to evaluate the significance of the prognostic variables.

Results: 80 pts (m/f: 46/34, median age: 41 years, range: 18−71 years) were enrolled. *MGMT* was assessable in 71 of 80 pts (88.8%), being methylated in 30 (42.9%) and unmethylated in 41 (57.7%) pts. Median PFS was 48.6 months (95% CI: 33.7−63.5), being 96 months (95% CI: 29−163) and 38 months (95% CI: 18.9−57.2) in *MGMT* methylated and unmethylated pts, respectively ($p = 0.09$). At univariate analysis, complete resection ($p = 0.02$), age ($p = 0.002$), and KPS ($p = 0.003$) were significantly correlated with PFS. At multivariate analysis only age remains correlated with PFS ($p = 0.01$). Median survival (OS) was 93.7 months (95% CI: 63.5−123.8), being not reached and 77 months (95% CI: 20−134.2), in *MGMT* methylated and unmethylated pts, respectively ($p = 0.03$). *MGMT* methylation ($p = 0.03$), age ($p = 0.0003$) and KPS ($p = 0.03$) were significantly correlated with OS at univariate analysis. At multivariate analysis, age ($p = 0.0002$) and *MGMT* methylation ($p = 0.01$) were correlated with a better OS.

Conclusions: *MGMT* methylation status is an independent prognostic factor together with age in AA. This datum should provide the background to improve the therapeutic index with temozolomide concurrent with and adjuvant to RT in AA.

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MGMT methylation status does not provide adjunctive prognostic information in pts with 1p/19q intact anaplastic gliomas

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Background: Chromosomes 1p/19q codeletion has been recognized as a prognostic and predictive factor in patients (pts) with anaplastic gliomas (AG). Non-codeleted (intact) anaplastic oligodendroglioma showed a survival comparable to that usually observed in pts with anaplastic astrocytomas; *MGMT* methylation status, moreover, has been found to be a prognostic factor in glioblastoma and anaplastic gliomas.

Methods: A retrospective analysis was made using a database of 253 AG pts followed prospectively between 01/1998 and 11/2008. We evaluated only pts who met the following inclusion criteria: age $\geqslant$18 years; PS 0−2; histological diagnosis of AG with 1p/19q intact, as determined by FISH analysis; treatment with postoperative radiotherapy (RT) and chemotherapy (CT); *MGMT* status determined using methylation specific PCR. The study aim was to evaluate the role of *MGMT* methylation status in 1p/19q codeleted AG pts. The log-rank test was used to evaluate the significance of the prognostic variables.

Results: 75 pts (m/f: 39/36, median age: 40 years, range: 18−70 years) were enrolled. Histology was anaplastic oligodendroglioma in 19 pts, anaplastic oligoastrocytoma in 22 pts and anaplastic astrocytoma in 34 pts; all these pts were 1p19q intact and received surgery, RT and CT. *MGMT* status, assessable in 66 pts (88%), was methylated in 38 pts (57.6%) and unmethylated in 37 pts (49.3%). Median progression-free survival (PFS) was 27 months (95% CI: 13.1−40.9). In multivariate analysis, no enhancement at time of diagnosis ($p = 0.03$) and gross total resection ($p = 0.04$) were significantly correlated with better PFS. Median survival was 74 months (95% CI: 55.9−92.1). In multivariate analysis, only age ($p = 0.005$) and KPS ($p = 0.045$) correlated with a better survival.

Conclusions: *MGMT* methylation status does not seem to provide adjunctive prognostic information in pts with 1p/19q intact AG.

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Immunological assessment of IL-2 effectiveness in chemotherapy in children with medulloblastoma

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The goal is to assess IL-2 immunological effectiveness during chemotherapy in children with medulloblastoma.

Patients and Methods: During induction chemotherapy, which included 4 cycles with vincristin, etoposid, cyclophosphamid, cisplatin or carboplatin, recombinant yeast interleukin-2 (Roncoleukin) was used based on the blind randomization method. Patients were divided into two groups depending on the presence of cytokine therapy in their treatment scheme: patients of the first group (I) received Roncoleukin the day before and during all 3 days of the induction chemotherapy (21 patients). The agent was given intravenously, in dose 1 million IU/m^2 during each chemotherapy cycle. Patients of the second group (II) did not receive biotherapy (21 patients). To assess Roncoleukin clinical effects, infectious complications were noted after each chemotherapy cycle and estimated according to CTC (Common Toxicity Criteria, NCI, Version 3.0, 2003). To assess Roncoleukin immunomodulating effect, lymphocyte subpopulation, T-lymphocyte activating markers expression and circulating cytokines level were investigated.

Results: The usage of IL-2 results in stable content of T-lymphocyte and its subpopulations during all chemotherapy cycles, whereas during chemotherapy without IL-2 substantial change in CD4+/CD8+ lymphocytes with the prevalence of CD8+ cells, as well as the increase of total portion of CD3+ lymphocytes and significant decrease of B-lymphocyte portion ($p < 0.05$) are observed. In the investigated groups, substantial increase of the portion of activated T-lymphocytes (CD3+HLA-DR+) occurs and more apparent changes are seen in the group of patients, that has not received IL-2 ($p < 0.05$). This tendency has also its effect on the inflammatory cytokine levels of TNF and IL-6. The portion of T-helpers expressing receptors for IL-2, relatively to the total T-helpers account, is characterized by its higher level in the group that received IL-2. At the beginning of IL-2 use, the quantity of infectious complications practically did not differ in both groups. By the fourth polychemotherapy cycle, infectious complications were lower more than by 3 times in the group of patients that received IL-2, than in the one without immunotherapy ($p < 0.05$).