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.

8723 POSTER

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.

8724 POSTER

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 ($p < 0.05$).

Conclusion: IL-2 in combination with polychemotherapy has immunomodulating effect, which considerably affects clinical effectiveness, allowing to decrease the frequency of infectious complications.

8725 POSTER

The safety and efficacy of intrathecal liposomal cytarabine in patients with carcinomatous meningitis from solid tumours

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Background: The purpose was to assess the efficacy and safety of liposomal cytarabine (LC) in the treatment of *de novo* carcinomatous meningitis from solid tumours.
Materials and Methods: From 2005−2008, unselected, sequential patients with solid tumours and de novo leptomeningeal involvement at 3 different Spanish institutions were offered treatment with intrathecal LC, subject to Spanish Ministry of Health approval (n = 16; 9 men, 7 women). None had previously received LC. The diagnosis was confirmed by cytology (n = 13), MRI (n = 10) and/or CT scan (n = 7). The LC treatment regimen was: (induction) 1×50 mg every 14 days (2 doses total), then (consolidation) 1×50 mg every 14 days (3 doses total), then (maintenance) 1×50 mg every 28 days (5 doses total). All patients received concomitant steroids as prophylaxis against arachnoiditis. Three also received concurrent systemic chemotherapy (2 concomitant, 1 sequential). Neurological response was defined as follows: Complete response (CR), improvement of all neurological symptoms; Partial response (PR), improvement of ⩾50% of neurological symptoms for ⩾2 weeks; Stable disease (SD), neurological symptoms unchanged; Progressive disease (PD), neurological symptoms progressed or proliferating. Cytological response (absence of malignant cells in the CSF) was assessed at the time of lumbar puncture for LC in patients who presented with positive cytology, and who received >1 dose of LC.
Results: Patients had a median age of 49 years (range 26−60) and a median follow-up of 42.5 days (range 4−414). All but 1 had undergone previous systemic chemotherapy, and 10 had also received previous radiotherapy. Primary tumours were: breast cancer 7, lung cancer 3, other tumours 6. The median number of LC doses received was 1 (range 1−6). A neurological CR was seen in 5 patients, a PR in 3, SD in 2, and PD in 7. A cytological response was sought in 5 and confirmed in 4, at 14, 19, 28, and 42 days, respectively. Median time to neurological progression or death was 14 days (range 0−170). Adverse effects were reported in 10/16 patients, but none was grade 4. The most frequently reported adverse effect was headache (6/16 patients).
Conclusions: In the largest European case series report to date to evaluate the efficacy and safety of LC in patients with carcinomatous meningitis from solid tumours, LC was generally well tolerated and efficacious. LC reduces the number of IT injections compared to conventional therapy, which should improve quality of life.

8726 POSTER

Clinical pattern of primary central nervous system lymphoma in a developing country

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Primary Central Nervous System (CNS) lymphoma is a rare entity. We wish to present our experience with this rare tumor.
Aim: To study the pattern of presentation and treatment results of Primary CNS Lymphoma from a single Institute in a developing country.
Materialand Methods: Thirty patients with a diagnosis of Primary CNS lymphoma were treated at Regional Cancer Centre, Trivandrum, India during the period 2000−2007. The case records of these patients were studied in detail with respect to their presentation, treatment and survival.
Results: Of the 30 patients, there were 18 males and 12 females. Their age ranged from 26 years to 76 yrs with a median age of 50 years. The main presentation was with features of raised intracranial tension and hemiparesis. The symptoms were present for a median period of 3 months. The pathologic subtype was predominantly Diffuse large B cell NHL in 26 patients, Burkitt lymphoma in 3 cases and diffuse small cell in 1. The main sites of involvement were frontal lobe, parietal lobe, frontopariental, temporal lobe, cerebellum and thalamus. Sixteen patients had undergone decompression. Fifteen patients received chemotherapy, of which 9 received single agent High dose Methotrexate, 5 patients received De Angeles protocol. Radiotherapy was given in 23 patients and the dose ranged from 45−55 Gy. At 2 years 10 patients were alive disease free and the longest survival was 90 months.
Conclusion: Primary CNS lymphoma a rare CNS tumor, is mostly large B cell subtype and requires multimodality management for disease free survival.

8727 POSTER

Outcome after high-dose methotrexate and radiotherapy for primary central nervous system lymphoma

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Background: To evaluate the outcome of patients with primary central nervous system lymphoma (PCNSL) after high-dose methotrexate (HDMTX)-based chemotherapy and radiotherapy (RT) and to identify prognostic factors for survival in this population.
Materials and Methods: Between March 2000 and July 2007, 43 patients with pathologically proven PCNSL received HDMTX based chemotherapy in conjunction with radiotherapy. HDMTX (2.5 g/m^2)-based chemotherapy was given in multiple cycles (median 5 cycle) at before or after RT. All the patients received whole brain irradiation (WBI), followed by boost to tumor bed. As for WBI, 25 patients were treated with reduced dose (median 30.6 Gy; range, 23.4−30.6 Gy) and 18 patients with average dose (median 36 Gy; range, 36−48.8 Gy).
Results: The median age was 55 years (range, 25−75 years) and the patients with poor performance status (PS) of 2 or higher on ECOG scale were 15. At a median follow-up of 26 months (range, 7−146 months), the median progression-free survival was 31 months and the median overall survival (OS) was 59 months. The 2- and 5- years overall survival (OS) was 68.62% ± 0.8% and 42.6% ± 0.9%. The old age (>50 years) and poor performance (ECOG⩾2) were associated with poor OS by univariate and multivariate analysis. There was no difference in survival and intracranial control between reduced and average dose WBI. ($p = 0.7808$ and $p = 0.2458$, respectively). Although marginally significant ($p = 0.0645$), the delayed neurologic toxicity of patients with reduced dose WBI were lesser compared with those with average dose WBI.
Conclusion: Reduced dose WBI could diminish the risk of treatment-related neurotoxicity without compromising survival in patients treated with HD-MTX based chemotherapy for PCNSL. In patients received HDMTX based chemotherapy, appropriate dose of WBI have to be further investigated in prospective trials.

8728 POSTER

The impact of the histology of primary tumor on RPA prognostic classifications in patients (pts) treated for brain metastases (BM) – retrospective analysis of 382 pts treated with hypofractionated whole brain radiotherapy (HWBRT)

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Background: The survival of patients with BM is strongly related to clinical prognostic factors included in the Recursive Partitioning Analysis (RPA) classes. [1] Histology of the primary tumor is not included in the RPA prognostic classes and it is unclear whether it influences survival. The aim of the study was to evaluate the impact of histology on the survival of BM patients among different RPA classes.
Materials and Methods: We performed a retrospective analysis of 382 pts with BM treated at our Institution between January 1995 and April 2008. 31%, 48% and 21% of them were respectively in RPA classes 1, 2 and 3. All were treated with HWBRT, 17% with the addition of surgery and adjuvant HWBRT. Radiotherapy doses were 30 Gy in 204 pts (53%) and 20 Gy in the remaining. The primary tumours were: breast cancer 87 pts (23%), lung adenocarcinoma 143 pts (37%), small cell lung cancer 42 pts (11%), kidney 14 pts (4%), melanoma 20 pts (5%), GE cancer 19 pts (5%), ovary/uterus 8 pts (2%), others 8 pts (2%), unknown 9 pts (2%), classified in broad categories in order to submit to statistical analysis larger groups. Uni- and multivariate analysis were performed.
Results: After a median follow-up of 146 days, the actuarial 1 year overall survival is 24%. Median survival in patients in RPA 1, 2 and 3 is respectively 269, 142 and 64 days (p = 0.0000). At univariate analysis the histology of primary tumor has a significant impact on median overall survival (OS) in each RPA class as shown in the following Table.