based on: 1) Absent NPAS3 expression is predominant in high grade astrocytomas, in comparison to low grade astrocytomas suggestive of an expression pattern typical of tumour suppressive-late stage progression factors. 2) Loss of function mutations of NPAS3, which are associated with a loss of heterozygosity of the NPAS3 locus are identified in glioblastomas. 3) Absent NPAS3 expression is predominant in >60% of malignant human glioma cell lines. 4) An over-expressed NPAS3 in malignant glioma cell lines suppresses the transformation potential, while the converse reduced expression promotes an increase in transformation potential. 5) A reduced NPAS3 expression (efficiency >90%) in concert with gliomagenesis pre-disposition genes transforms a well characterized TERT immortalized human astrocyte cell line and promotes the growth of malignant astrocytomas, while an over-expressed NPAS3 suppresses the transformation. 6) NPAS3 drives tumour progression by the control of cell cycle, proliferation, apoptosis, migration/invasion and angiogenesis.
Conclusions: Our data provide findings of NPAS3 as a novel gene which drives the progression of malignant astrocytomas, with tumour suppressive roles. We believe that this body of work is highly significant in our quest to better understand the biology of astrocytomas, and with prospects for improved targeted therapies in the treatment of this currently and relatively incurable disease.

8714 POSTER

Tamoxifen Interaction With Protein Kinase C Delta

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Background: Tamoxifen, selective estrogen receptor modulator, is efficient in the treatment of some brain cancer tumours. This effect is thought to be related with tamoxifen influence on protein kinase C (PKC) and mechanism of antiestrogen influence on the enzyme is still unclear. We have supposed that direct tamoxifen interaction with PKC could be one of the reasons of the antiestrogen therapeutic activity in brain tumours.
Materials and Methods: A549 human non-small-cell lung cancer cells were studied by flow cytometry and fluorescent microscopy. A549 cells were incubated with Abcam antibodies: primary (PKC delta, EP1484Y or rabbit IgG) for 1.5h and with secondary FITC-conjugated antibody (ab6108) for 1.5 h. The important feature of the primary anti-PKC antibody is that the epitope resides near the C-terminus of the protein, where catalytic domain of enzyme is located.
Results:
1. It was revealed PKC delta expression in about 70% of the A549 cells in culture.
2. Tamoxifen pretreatment decreased significantly both the mean cell specific fluorescence (in about 1.6 times) and the specific stained cells number (up to 40%) after incubation with anti-PKC delta antibody.
3. In the microscopic visualization of the tamoxifen effect on specific antibody interaction with the A549 cells the result was the same: the cell specific fluorescence intensity as well as specific stained cells number after tamoxifen pretreatment were decreased significantly.
4. Tamoxifen didn't influence the isotypic antibodies interaction with the cells and didn't change the cell autofluorescence.

Conclusion: Decrease in the mean cell fluorescence intensity under tamoxifen pretreatment shows disturbed availability of the PKC delta catalytic domain to antibody binding, most likely because of the antiestrogen interaction with the PKC delta molecule. Because specific triphenylethylene-binding site is located near the catalytic domain of the PKC, there is high probability that the tamoxifen interaction with the PKC delta results in the modification of the enzyme catalytic activity and changes regulation in downstream signaling pathways of the PKC delta. We believe that tamoxifen interaction with the PKC delta could be one of the reasons of the antiestrogen therapeutic activity in some brain cancer tumours.
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8715 POSTER

Comparison of Instruments for Quality of Life Measurement in Bulgarian Patients With Malignant Glial Tumours

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Background: Measuring the quality of life (QoL) has become an integral part of initial examination, choosing a therapeutic approach and for the follow-up of the neurosurgical treatment. Most commonly used questionnaires for QoL are SF-36 (Short-Form Health Survey), QLQ-C30 of the European Organization for Research and Treatment of Cancer (EORTC) and World Health Organization Quality of Life-100 (WHOQOL-100). Sofia Self-Assessment Scale (SoS-SAT) is a newly developed in Bulgaria questionnaire for QoL assessment. SoS-SAT is self-directed, mainly to patients with supratentorial processes and consists of 12 questions (5 related to physical functioning and the presence of neurological symptoms, 7 related to QoL and symptoms of depression). The objective of our study was to evaluated applicability of aforementioned instruments for measuring QoL in Bulgarian patients with malignant gliomas.
Material and Methods: In the present study 100 patients with malignant gliomas treated in the period 2003–2005 were included. QoL was measured through the SF-36 (n = 95), SoS-SAT (n = 45), QLQ-C30 (n = 40) and WHOQOL-100 (n = 35) before and after treatment. All patients were asked to answer 5 questions related to ease of completion, clartiry and comprehensiveness of each used in this study QoL questionnaires.
Results: The studied questionnaires demonstrate that all of them are clearly formulated and relevant to the health of patients with malignant gliomas. 60% of patients found WHOQOL-100 instrument more difficult to complete than others. Averaged results of this study revealed that SF-36, QLQ-C30 and SoS-SAT seems to be more appropriate for measuring QoL in patients with malignant gliomas − 80% of the patients did not have any difficulties with questions clarity or questionnaires completion. Also SoS-SAT is the instrument to which most patients show positive attitude in comparison of other.
Conclusions: The SF-36, QLQ-30 and SoS-SAT questionnaires are the most suitable existing instruments for QoL assessment in Bulgarian patients with malignant gliomas.

8716 POSTER

Novel Features That Impact the Outcome of Patients With Glioblastoma Multiforme − Multivariate Analysis From a Comprehensive Dataset

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Background: Glioblastoma multiforme (GBM) is the most common malignant adult brain tumour. While the impact of variables such as age and performance status on outcome is well known, the potential impact of other variables such as socio-econonomic status and clinical trial participation to date have not been well explored.
Materials and Methods: Data on patients (pts) with GBM were accessed from a prospective neuro-oncology dataset collected over 12 years (1998–2010) at two institutions (one public, one private). Death data were obtained from the state Cancer Registry. Data linkage and analyses were performed by BioGrid Australia. Both univariable and multivariate logistic regression analyses were performed to look for relationships between clinical and socio-demographic variables and overall survival.
Results: In total 541 pts were evaluated; the median age was 60 years. Sixty-five patients (12%) were enrolled in a clinical trial. In univariable analysis, positive predictors for longer survival were: clinical trial participation (HR for death 0.43, 95% CI 0.33–0.60, $p < 0.0001$), higher IRSAD (index of relative socio-economic advantage and disadvantage) score (socioeconomically advantaged) (HR 0.85, 95% CI 0.8–0.95, $p = 0.0093$), macroscopic resection versus biopsy alone (HR 0.5, 95% CI 0.4−0.6, $p < 0.001$), and more than one operation (HR 0.5, 95% CI 0.4−0.6). Older age (HR for death 3.0, 95% CI 2.4−3.7, $p < 0.0001$), worse ECOG performance status (HR 1.5, 95% CI 1.3−1.7, $p < 0.0001$) and multifocal disease (HR 1.5, 95% CI 1.2–1.97, $p = 0.001$) were significantly associated

with inferior overall survival. Gender, country of birth, smoking status and diabetes did not significantly impact on survival. Multivariate analysis showed that age, clinical trial participation, IRSAD score and ECOG performance status were all independent predictors for overall survival.
Conclusions: This is the first study to demonstrate a profound effect of clinical trial participation, regardless of treatment arm and independent of age and performance status; and socio-economic status on survival in patients with GBM. The reasons why more socio-economically disadvantaged patients have shorter survival is unknown. These are novel and intriguing findings that require further exploration and could be used to help inform and improve best clinical management of patients with GBM.

8717 POSTER

Application of IMRT Technique in Treatment of Malignant Gliomas. Assessment of Treatment Tolerance

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Background: Assessment of tolerance of combined modality therapy of patients with malignant gliomas irradiated using IMRT technique. We compared dose distribution in IMRT and conformal 3D treatment plans.
Materials and Methods: Between 2009 and 2010 in the Oncology Center in Krakow 17 patients with malignant gliomas received combined modality treatment. Mean age was 53 years (range 28−66 years). All patients were in good performance status (WHO 0−1). There were 15 patients with glioblastoma multiforme and 2 with anaplastic astrycytoma. Ten patients underwent complete resection and 7 partial resection. Patient were irradiated using IMRT technique with a total dose of 60 Gy in 30 fractions. All patients concurrently received temozolamide in the dose of 75 mg/m^2. In all patients we performed additional plans using 3D conformal radiotherapy (3D-CRT) techniques and compared with IMRT plans. The 3D-CRT plans were prepared using 3−4 fields and IMRT plans consisted of 7−8 fields. The primary objective was to treat the planning target volume and to minimize the dose to organs at risk (OAR). Volumetric analysis, target coverage and conformity of prescribed doses were used in plan comparison.
Results: Treatment tolerance was vary good in all patients. Only 4 patients needed steroids during treatment. Adjustment of the dose distribution to the target volume was improved and the critical structures were better spared in the IMRT plans than in 3D-CRT plans. For all patients the mean dose and the maximum dose to OAR were significantly reduced in IMRT plans. With respect to target volume, IMRT technique reduced the maximum dose while increasing the minimum dose, resulting in improved conformity. In same patients with tumours located very close to OAR it was impossible to give 60 Gy for target volume with 3D-CRT technique because of not acceptable doses in OAR.
Conclusions: The IMRT technique combined with concurrent temozolamide is well tolerated and offers significant advantages comparing to 3D-CRT. Application of IMRT allows dose reduction at OAR without compromising target coverage.

8718 POSTER

Influence of Presenting Symptoms on Treatment Patterns and Outcomes in Glioblastoma Multiforme (GBM)

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Introduction: GBM is an aggressive disease with poor outcome despite multi-modality treatment. Presentation is highly variable, ranging from neurological deficits and seizures to generalised symptoms of raised intracranial pressure such as headaches. We sought to review presenting symptomatology of GBM in a neuro-oncology referral centre, and the potential influence on management and outcome.
Methods: A prospectively maintained institutional database was reviewed to identify patients (pts)with diagnosis of GBM. Cliniopathologic data were analysed. Presenting symptoms were stratified into: neurological deficit (Def), headaches (HA) or seizures (Seiz), and one, two or three symptoms. Debulking and optimal adjuvant therapy rates were compared with chi^2 test, overall survival was compared with log-rank test method. Comparisons were made across stratified groups, e.g. HA vs no HA.
Results: Between Sept 2004 and Dec 2009, 121 evaluable pts were identified. Median age at diagnosis was 59 years (range 18−76) and 74% (n = 90) of pts were males. Common sites of tumours were parietal (28%), frontal (22%) and temporal (21%) lobes, with left hemisphere predominance (51%). In total, 81 pts (67%) presented with one symptom: neurological Def 46 (38%), HA 22 (18%) and Seiz 13 (11%), while 40 (33%) presented with two symptoms: Def + HA 27 (22%), Def + Seiz 10 (8%) and HA + Seiz 3 (2%). No pts had all 3 symptoms at presentation. Comparing pts with 1 vs 2 symptoms, rates of debulking were 65.4 vs 67.5%, p = 0.84 and rates of optimal therapy were 64.2 vs 60%, p = 0.69 [4 and 2 pts were not treated, respectively − see Table]. Hazard ratio for overall survival between groups was 0.71 (CI 0.49–1.34, p = 0.08). 52 pts (43%) had HA at presentation. Debulking (71 vs 62%, p = 0.39) and optimal treatment rates (62 vs 65%, p = 0.71) were similar. HR for overall survival was 1.08, p = 0.69.
Conclusion: Our data shows that the majority of pts (81%) with GBM presented with at least 1 symptom, neurologic Def being the most common. We have also shown that presenting symptoms have no significant influence on management or outcome. Time from onset of symptoms to diagnosis may be a confounder, however, as treatment may be instituted earlier. We intend to examine this.

	Debulked	%	Optimal Adjuvant Tx	%	Suboptimal Adjuvant Tx	%	No Adjuvant Tx	%	Total
HA	14	64	15	68	6	27	1	5	22
Def	29	63	30	65	14	30	2	4	46
Seiz	10	77	7	54	5	38	1	8	13
	53	65	52	64	25	31	4	5	81
Def + HA	22	81	16	59	10	37	1	4	27
Def + Seiz	4	40	6	60	4	40	0	0	10
HA + Seiz	1	33	2	67	0	0	1	33	3
	27	68	24	60	14	35	2	5	40

8719 POSTER

Long-term Follow-up in Adult Patients With Low-grade Glioma (WHO II) Postoperatively Irradiated. Analysis of Prognostic Factors

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Background: There is little consensus about the optimal treatment for low-grade glioma (LGG), and the clinical management of LGG is one of the most controversial areas in neurooncology. Radiation therapy is one option for treatment of patients with LGG whereas other options include postoperative observation. The aim of this study is to report the long-term follow-up of a cohort of adult patients with LGG post-operatively irradiated in one institution, and to identify prognostic factors for progression free survival.
Material and Methods: Between 1975 and 2005, 180 patients with LGG (WHO II) received postoperative irradiation after non radical (subtotal or partial) excision. Patients had to be 18 years of age or older, and have histologic proof of supratentorial fibrillary (FA), protoplasmic (PA) or gemistocytic astrocytoma (GA). Radiotherapy was given within 3 to 10 weeks after surgery. The treatment fields were localized and included the preoperative tumour volume, with a 1−2 cm margin, treated to a total dose of 50 to 60 Gy in 25 to 30 fractions over 5 to 6 weeks.
Results: Actuarial ten- year progression free survival (APFS) in the whole group was 19%. The worse prognosis was reserved for patients with GA. Ten-year APFS rates for GA, PA and FA were 10%, 18% and 22% respectively.
Conclusion: The findings from our long-term cohort of 180 patients with LGG confirmed by uni- and multivariate analysis demonstrated that only astrocytoma histology significantly determined the prognosis. The best survival is reserved for patients with the fibrillary variant, and the worst for the gemistocytic one.

8720 POSTER

Positive Osteopontin Expression in High Grade Gliomas Predicts Poor Prognosis

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Background: Hypoxia associated proteins are of particular interest because of recent advances in targeted therapy. High expressions of hypoxia-inducible factor-1α (HIF-1α) and carbonic anhydrase IX (CA IX) appear to be strong prognostic indicator in many malignancies, however their role is unclear in high grade gliomas. Moreover, one of the other novel hypoxia-regulated molecule-osteopontin (OPN)-may play a role in high grade gliomas and may provide further therapy options. We performed an immunohistochemical analysis of OPN, HIF-1α and CA IX and correlated their expression levels with patient survival.
Material and Methods: A total of 92 (40 female, 52 male) patients with WHO grade 3 (n = 19) and grade 4 (n = 73) were included in the study. The median age was 49 (18−77) years. Gross total resection had