Methods: Sixty milimolar NaB was continuously administered intrathecally to 23 patients (pts) with recurrent or progressive MG using a balloon pump system and treatment was continued as long as possible by changing the pump containing NaB weekly. MCT1 expression was also examined by immunohistochemical staining with specific rabbit polyclonal anti-bodies in the center of the tumor and the brain tissue surrounding the tumor in specimens obtained just before commencement of CIA of NaB in 18 pts with recurrent or progressive MG, and the correlation of MCT1 expression with clinical response was evaluated.
Results: Sixteen of 20 evaluable pts showed anti-tumor effects including tumor regression in 11 pts. The overall median survival time of MG was 11.0 (330 days) months. Four of 5 pts with CSF tumor cell dissemination showed a therapeutic response, including temporary negative cytological conversion. However, specimens in all pts responded to the therapy showed marked MCT1 expression in the tumor. By contrast, 4 pts, who did not respond to therapy, showed a low grade of MCT1 expression in the tumor.
Conclusion: The present therapy was well tolerated, resulted in long-term inhibition of tumor growth in some pts, and showed therapeutic safety. The most important favorable factor influencing the response to CIA of NaB was high grade of MCT1 expression in the nucleus and cytoplasma in the center of the tumor.

8737 POSTER

High resolution analyses of loss of heterozigosity (LOH) of chromosome 22 by SNP-arrays and microsatellite markers in meningiomas

M.D. Tabernero[1], C. Diez-Tascón[2], A. Maíllo[3], A. Castrillo[3], P. Sousa[3], M. Merino[3], A. Orfao[4]. *[1]IECSCYL-Hospital Universitario-Centro de Investigación del Cáncer IBMCC/CSIC-USAL, Unidad de Investigacion, Salamanca, Spain; [2]Hospital Virgen Blanca de León, Servicio de Anatomía Patológica, León, Spain; [3]Hospital Universitario de Salamanca, Servicio de Neurocirugía, Salamanca, Spain; [4]Centro de Investigación del Cáncer IBMCC/CSIC-USAL- Universidad de Salamanca, Servicio General de Citometria Departamento de Medicina, Salamanca, Spain*

Background: The most frequent chromosomal losses in meningiomas affect the long arm of chromosome 22. Several molecular technologies have been applied to find candidate genes in this chromosome. Microsatellite markers PCR analysis has been used to determine loss of heterozigosity (LOH) and actually single nucleotide polymorphisms (SNPs) arrays are avalaible to search LOH regions, that is consider a key event in the origen of many cancers. Our objective were to perform a genome wide study of LOH of chromosome 22 in meningioma patients using SNP-arrays and results validate with microsatellite markers.
Material and Methods: In the present study, chromosomal 22 LOH regions were analyzed by SNP-arrays in 50 meningioma paired samples with a total of 200 arrays and microsatellite markers were used in a group of tumors too.
Results: The genotype data of 6206 SNPs located on chromosome 22 with an average distance between SNP of 5.8 Kb was obtained. LOH regions were identified in 15 out of 50 cases combining SNP calls of pair normal and tumor samples. The other two third of cases did not presented any LOH region in chromosome 22. The results were verified using a independent method based on microsatellite markers PCR analysis with 8 markers – D22S535, D22S929, nf2CAV, D22S1172, D22S1162, D22S1156, D22S417 and D22S1056 – located in MN1(22q12.1), NF2 (q12.2), LARGE (q12.3), CARD10 (q13.1), FAM152B (q13.2), POLR2F-SOX10 (q13.1), A4GALT (q13.2), ARHGAP8 (q13.31) and TTL8 (q13.33) genes, in a subset of 15 tumors. LOH frequency were higher with PCR microsatellite study than SNP-arrays and both techniques present a high concordance. All cases were informative for more than half of the microsatellite markers analyzed (>5 loci to 11 loci)
Conclusions: In summary, SNP approach allowed extensively map LOH region of chromosome 22 in meningioma tumors. In contrast to diploid tumors (only one present LOH in 1 locus) LOH was a frequent finding in meningiomas with chromosome 22 losses.

8738 POSTER

Efficacy of glycopeptide cancer vaccine with adjuvants for treatment of intracranial transplanted melanoma B16

O.V. Mazur[1], V.O. Schlyakhovenko[1], S.V. Olishevsky[1], O.Y. Glavacky[2]. *[1]R.E. Kavetsky IEPOR National Academy of Sciences of Ukraine, Tumor Enzymology, Kyiv, Ukraine; [2]A.P. Romodanov Institute of Neursurgery Medical Academy of Sciences of Ukraine, Neurooncology, Kyiv, Ukraine*

Introduction: Despite recent advances in conventional surgical treatment, chemo- and radiotherapy innovative strategies are urgently needed for the successful treatment of brain cancer patients. Consequently, efforts aimed at developing new therapies have focused on new treatment strategies directed on disease elimination, tumor recurrence prevention and inhibition of metastatic dissemination. Cancer vaccines and adjuvants provided the important tools for manipulation of the immunological response to tumors, and therefore can be considered as one of the best alternative to high-toxic conventional anticancer therapies. The main goal of present study was to investigate the efficacy of glycopeptide cancer vaccine (gp50) alone and with adjuvants for therapeutic treatment of intracranial transplanted melanoma B16.
Materials Methods: The gp50 composed of originally prepared autologous 50 kDa-glycopeptide antigens was triply s.c. injected to C57Bl/6 mice with intracranial transplanted melanoma B16. Bacterial CpG DNA (bCpG DNA) and vitamin complex (VC – vitamins C and K_3 in ratio 100:1) were used as vaccine adjuvants. Mice from control group received injections of physiologic saline. The efficacy of immunotherapeutic treatment was evaluated using survival rates of tumor-bearing mice; and cytotoxic activity of splenic lymphocytes and histological examination of changes in mouse brain during vaccinotherapy.
Results: Administration of gp50 alone or combined with bCpG DNA or VC resulted in marked antitumor effect. Median survival rate of mice treated with gp50 alone and combined with bCpG DNA or VC were 27.7 ± 8.0 and 24.6 ± 4.9, 26.0 ± 6.9 days respectively compared with only 13.7 ± 3.8 days in control group. In mice from all treated groups significant increase of lymphocyte cytotoxic activity was also observed. Histological analysis of brain sections showed significant inflammatory lymphocyte infiltrates around tumor masses and necrotizing areas of melanoma cell in brain of mice injected with gp50 alone or with adjuvants as compared with control mice.
Conclusion: Present results suggest that application of gp50 alone or combined with such adjuvants as bCpG DNA and VC can be promising strategy for successful treatment of intracranial tumors.

Lung cancer

Oral presentations (Mon, 21 Sep, 11:00−12:45)

Lung cancer I

9000 ORAL

Mutations of EGFR (mEGFR) in tumour tissue and serum DNA from stage IV non-small-cell lung cancer (NSCLC) patients (p) prospectively treated with erlotinib

R. Rosell[1], B. Massuti[2], M. Cobo[3], A. Sala[4], R. Blanco[5], S. Catot[6], I. De Aguirre[7], C. Queralt[7], C. Mayo[8], M. Taron[1]. *[1]Catalan Institute of Oncology Hospital Universitari Germans Trias i Pujol, Oncology Service, Badalona (Barcelona), Spain; [2]Hospital General de Alicante, Oncology Service, Valencia, Spain; [3]Hospital Carlos Haya, Oncology Service, Malaga, Spain; [4]Hospital de Basurto, Oncology Service, Bilbao, Spain; [5]Hospital de Terrassa, Oncology Service, Terrassa, Spain; [6]Hospital Althaia, Oncology Service, Manresa, Spain; [7]Catalan Institute of Oncology Hospital Germans Trias i Pujol, Oncology Service, Badalona Barcelona, Spain; [8]Pangaea Biotech Institut Universitari Dexeus, Oncology Service, Barcelona, Spain*

Background: We evaluated mEGFR in tumor and matched serum at baseline and assessed their role in a multicenter trial of first- and second-line erlotinib in stage IV NSCLC p with mEGFR in tumor.
Material and Methods: mEGFR were detected in 350 of 2105p (16.6%) screened. 217p with mEGFR received erlotinib; 79 did not due to patient or physician decision. mEGFR were assessed in paired serum samples from 164 p with mEGFR in tumor for whom baseline blood samples were available. mEGFR testing in both tumor and serum was performed centrally. EGFR exon 19 deletions (del 19) were studied by length analysis of fluorescently labeled PCR products and the exon 21 L858R by a PCR Taqman assay.
Results: Overall response rate was 70%, time to progression (TTP) was 14 months (m), and median survival (MS) was 27 m. mEGFR status in the serum matched that in the tumor tissue in 97/164 p (59.1%), in 44.1% of p with PS 0, in 57.4% of p with PS 1, and in 78% of p with PS 2 ($P = 0.01$). There were no differences in the metastatic patterns either according to the presence of mEGFR in serum or according to the type of mEGFR. Response rate was 69.8% in 67 p without mEGFR in serum and 71.7% in 97 p with mEGFR in serum. TTP was 19 m for p with mEGFR only in tumor and 12m for p with mEGFR in tumor and serum ($P = 0.14$). TTP for p with del 19 only in tumor was 22 m vs 13 m for p with del 19 in both tumor and serum ($P = 0.36$). TTP for p with L858R only in tumor was 16 m vs 11