pared to those without amplification, indicating a similar dynamic range between the two methods. Similarly, a high concordance was observed between both methods for detecting EGFRvIII expression. Complete transfection analysis and profiling showed that genes such as PIK3CA and PTEN were regulated by EGFR signaling were not differentially expressed between responders and non-responders. However, an increased expression of T-cell markers, such as CD2 (p<0.0001) and CD3E (p=0.003), was observed in responders versus non-responders. Further analysis is ongoing in additional tumor samples.

CONCLUSIONS: A high degree of concordance between RNAseq and qRT-PCR indicates that RNAseq can be used effectively in future ABT-414 studies to determine EGFR status in FFPE tissues. An increased expression of immune markers in responders suggests a role of immunological factors in influencing response to ABT-414 therapy in GBM patients.

P06.03 ANAPLASIC OLIGODENDROGLIOMA AND Oligoastrocytoma without 1p-19q Co-deletion: A Mono-institutional Retrospective Study A. Silvani, F. Gavigni, G. Simonetti, A. Innocenti, M. Farnotti, G. Finocchiaro, E. Lamperti, A. Botturi, B. Pollo, F. DiMeoco Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy.

Allelic losses of chromosomes 1p and 19q in patients with anaplastic oligodendroglioma(AOD) and oligoastrocytoma(AOA) represent a strong prognostic factor and a powerful predictor of survival. This subset of patients benefit from the addition of chemotherapy(CT) to radiotherapy(RT) with a significant improvement of overall survival(OS) and progression-free survival(PFS). In patients without 1p19q co-deletion, there are no standard-of-care and conflicting opinions impose to review the possible therapeutic approach. A total of 214 patients with histological proven of AOD and AOA treated in our institution over the last 10 years were evaluated. Eighty patients were eligible for loss-of-heterozygosity (LOH) evaluation. The absence of 1p19q co-deletion was confirmed in 33 patients. Clinical and genetic data, treatments and survival assessment were described and discussed. In non-co-deleted group, m-OS and m-PFS were respectively 38,4 months (95% CI 21,99-59,77) (P=0,018) and 16 months (95% CI 13,0-20,0). On the other hand, m-OS of the whole group was 59,7 months. Concerning treatments, therapeutic approach has been variable with a percentage in RT and concomitant temozolomide in the past two years. In 6% of patients CT was considered as first-line treatment after surgery. Data confirmed the prognostic role of LOH, with the most advantages for patients with co-deletion. Regarding therapeutic approaches, results showed a quite aggressive attitude in our clinical practice. The choice between RT or CT as first line treatment after surgery do not seem to influence the prognosis.

P06.04 MUTATION ANALYSIS OF THE ISOCITRATE DEHYDROGENASE 1(IDH1) GENE USING CELL FREE DNA FROM THE CEREBROSPINAL FLUID (CSF) OF GLIOMA PATIENTS J. Adachi, K. Watanabe, T. Suzuki, K. Mishima, T. Fujimaki, R. Nishikawa Department of Neurosurgery/NeuroOncology, Saitama Medical University International Medical Center, Hitada, Saitama, Japan.

BACKGROUND: Mutation in the IDH1 gene is a genetic defect exclusively found in glioma as a mutation in solid tumors, and has been established as a prognostic factor for WHO Grade 2-4 glioma. Therefore, detecting this mutation is clinically important. In this study, we report the results of analyzing defects in the IDH1 gene by detecting circulating cell free (ccf) DNA in the CSF derived from the tumor tissue of glioma patients. METHODS: Lumbar puncture was performed to obtain CSF from 7 patients with glioma. ccfDNA was extracted from 1 ml of CSF using the Maxwell rapid sample concentrator system. Subsequently, the presence of point mutation of the IDH1 gene at codon 132 was screened by real-time PCR/high-resolution melting curve analysis, and the mutation was confirmed on the basis of DNA sequencing results. Status in the IDH1 gene mutation was further confirmed on the basis of DNA sequencing results. Results of analyzing defects in the IDH1 gene by detecting circulating cell free DNA from the surgically excised tumor tissue were consisted in all patients. However, IDH1 gene mutations was not detected all in plasma-derived ccfDNA. CONCLUSION: Therefore, gene analysis of ccfDNA from the CSF, not from the plasma, enabled the evaluation of IDH1 gene defect in glioma patients less invasively, without directly obtaining any tumor tissue. Moreover, this technique can be applied to analyze molecular markers other than the IDH1 gene, such as MGMT gene promoter methylation.

P06.05 MYOINOSITOL AS A PREDICTIVE BASELINE BIOMARKER FOR OVERALL SURVIVAL OF PATIENTS WITH RECURRENT GLIOBLASTOMA TREATED WITH BEVACIZUMAB: A 1H-MAGNETIC RESONANCE RESONANCE STUDY E. Steidl1, O. Pilatus2, J. P. Steinbach1, F. Zanella1, M. W. Romellenteisch1, E. Hattingen2, O. Bahr1,1

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BACKGROUND: Antiangiogenic treatment of glioblastoma with Bevacizumab (BVZ) lacks predictive markers. Myo-inositol (MI) is an organic osmolyte, with intracellular concentration changes depending on the extra-cellular osmolality. Since BVZ markedly reduces tumor edema, we asked whether the MI concentration in the tumor changes during therapy. METHODS: We used 1H-MR spectroscopy to measure the MI concentrations in the tumor and contralateral control tissue of 39 prospectively recruited patients with recurrent glioblastomas before and 8–12 weeks after starting therapy. 30 patients received BVZ and 9 patients were treated with CCNU/VM26 as control. We performed a survival analysis to evaluate MI as a predictive biomarker for BVZ therapy. RESULTS: MI concentrations increased significantly during BVZ therapy in tumor (p<.001) and control tissue (p<.001), but not during CCNU/VM26 treatment. For the BVZ cohort, higher MI concentrations in the control tissue at baseline (p=0.001) and higher differences between control and tumor tissue (delta MI, p=0.011) were associated with longer survival. A Kaplan-Meier analysis showed a median OS of 164 days for patients with a deltaMI < 1,817 mmol/L and 273 days for patients with a deltaMI > 1,817 mmol/L. No differences were observed for the relative changes or the post treatment concentrations.

CONCLUSION: Pre-therapeutic MI concentrations are predictive of overall survival in patients with recurrent glioblastoma treated with BVZ. Our data confirm that recurrent glioblastoma show a strong metabolic reaction to BVZ. Further, our results support the hypothesis that MI might be a marker for early tumor cell invasion.

P06.06 IS ACTIVATING TRANSCRIPTION FACTOR 5 (ATF5) A NEW THERAPEUTIC TARGET IN ASTROCYTOMAS OF DIFFERENT WHO GRADES AND VARYING BIOLOGICAL BEHAVIOR? AN EXPRESSION ANALYSIS J.A. Feldheim, A. F. Kiebler, T. Linsenmann, R. Ernestus, M. Löhrt, C. Hagemann University of Würzburg, Department of Neurosurgery, Tumorbiology Laboratory, Würzburg, Germany.

OBJECTIVE: Activating transcription factor 5 (ATF5), a widely expressed basic leucine zipper protein, suppresses differentiation of neuroprogenitor cells into glial or neuronal in the normal brain (NB). It has been reported to be overexpressed in glioblastoma (GBM). A reduction of ATF5 expression or activity in GBM cells leads to p53-independent apoptotic cell death, therefore suggesting that it might serve as a novel therapeutic target. However, to our knowledge, no data on ATF5 expression in low grade astrocytomas (LGA) or recurrent GBM has been published so far. Therefore, we aimed to examine the ATF5 expression in patients’ astrocytoma samples of different WHO grades and varying biological behavior.

METHODS: ATF5 mRNA expression was measured by quantitative PCR (qPCR). The mRNA was extracted from cell lines U87, GaMG, U343, DKM, SNB19, and U138 and from frozen samples of patients’ GBM (n=15), LGA (n=12) and NB (n=4). In addition, an independent panel of GBM with varying biological behavior, i.e. GBM with local growth and local relapse (local primary tumor (LP): n=26; local relapse (LR): n=8), GBM with local growth and multifocal relapse (primary tumor (PMR): n=12; relapse (RMR): n=3), and GBM with a multifocal primary growth pattern (MPP; n=9) was examined. Data were analyzed using unpaired two-sided t-test.

RESULTS: A nearly 12 times overexpression of ATF5 mRNA was observed in LGA (p<0.004), as well as GBM (p<0.001) compared to NB. The subgroup analysis revealed a significant increase of ATF5 expression in LP (p=0.013), LR (p=0.041), PMR (p=0.018), and MP (p<0.012). However, no difference could be detected between primary tumors and local (p=0.572/multifocal relapse (p=0.577). Primary tumors LP, PMR and MP displayed a similar ATF5 expression (p>0.05). Among the analyzed GBM cell lines U343 cells showed the strongest expression.