Abstracts

P04.07. EXPRESSION PROFILE OF ANGIOGENIC FACTORS IN PAIRED INITIAL AND RECURRENT GLIOBLASTOMA

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BACKGROUND: Angiogenesis is one of the key features of Glioblastoma (GB). Our objective was to identify the changes in the expression of angiogenic factors in GB after radio-chemotherapy.

METHODS: Analysis of all patients with available frozen tumor material from initial and recurrent surgery for GB treated with chemo-radiotherapy (CTRT) in first line setting in our institution between 2003 and 2009. Molecular screening was realized using two types of RT2Profiler PCR arrays (Qiagen). The RNA expression profile of selected genes was validated using quantitative RT PCR. Protein expression was analyzed by immunohistochemistry (IHC). Explants of newly GB were treated with temozolomide, radiotherapy and anti-CXCR4 (AMD3100).

RESULTS: Twenty nine patients were included with median age of 57.1 years (37.2-74.1). The RT2Profiler PCR arrays results allowed a selection of seven genes: VEGFA, VEGFR2, VEGFR1, Adrenomedullin, SDF1, CXCR4, and HIF1α. The steady state levels of CXCR4 RNA at recurrence was significantly increased (p = 0.029) while HIF1α RNA was significantly decreased (p = 0.009). A trend for a decrease of VEGFR2 RNA (p = 0.081) and an increase of SDF1 RNA (p = 0.107) was observed. Changes of SDF1 RNA tended to be correlated to changes of CXCR4 RNA (p = 0.077) and inversely correlated to changes of HIF1α RNA (p = 0.064). By IHC, VEGFR2 staining was significantly decreased at recurrence (p = 0.004) while SDF1 expression tended to increased (p = .096). Medians initial and at recurrence overall survival (OSI and OSR) of this selected population were 25.5 (95% confidence interval (CI) 17-34) and 11.4 (95%CI 9-13.9) months respectively. By multivariate analysis, VEGFR2 RNA initial and at recurrence levels were significantly correlated to OSI (p = 0.019, Hazard ratio (HR) = 3.650) and OSR (p = 0.024, HR = 2.536) while HIF1α RNA level at baseline was correlated to OSI (p = 0.012, HR = 0.300). In newly GB explants, a higher anti-tumoral effect was observed with the combination of AMD3100 and CTRT versus CTRT alone.

CONCLUSION: Acquired resistance of GB to chemo-radiation could be associated with a switch of angiogenic pattern from VEGFR2-HIF1α to SDF1-CXCR4 pathway, leading to new perspectives in angiogenic modulation and GB treatment.