AI-28. RECURRENT GlioBLASTOMAS AFTER TREATMENT WITH BEVACIZUMAB
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Bevacizumab, a humanized monoclonal antibody to vascular endothelial growth factor, has been evaluated in the treatment of patients with primary or recurrent glioblastoma. We aimed to characterize neuropathological and molecular features in recurrent malignant gliomas after failure of Bevacizumab treatment. We evaluated 11 patients with high-grade astrocytomas (10 glioblastomas, 1 anaplastic astrocytomas) before and after Bevacizumab treatment. Clinical records and neuroimaging findings were retrospectively reviewed for each patient. Histological features included morphology, vessel density, cellularity and proliferation. Immunohistochemical studies were performed for selected signaling molecules, including cMET, phosphoAkt, phosphoRPS6K, phosphoMET, phosphoMAPK (ERK1/2), phosphoSTAT3 and phosphor-mTOR. In addition, we performed a gene amplification analysis of cMET. As a reference cohort, primary and recurrent tumors from 22 patients with high-grade astrocytomas (21 glioblastomas, 1 anaplastic astrocytoma) without Bevacizumab treatment were studied.

Radiographic recurrence occurred most often at the initial tumor site in both patient groups. Histologically, most recurrences after Bevacizumab treatment showed reduced vessel density and less prominent microvascular proliferation as compared to the corresponding primary tumors. Whereas most investigated signaling molecules showed variable results, expression of cMET protein was upregulated in 6/10 patients following Bevacizumab treatment. In addition one recurrent tumor after Bevacizumab treatment showed MET gene amplification. Based on our data set, a common feature after bevacizumab treatment is altered vascular morphology and upregulation of cMET protein expression. Thus, therapeutic strategies combining VEGF and cMET inhibition may augment clinical efficacy over VEGF inhibition alone in glioblastoma.