Underwent a postoperative course of conformal chemoradiotherapy targeting doses (TTD) of 54-60 Gy, and 147 patients in 2007-2011 had pathological diagnoses of grade III anaplastic astrocytoma (AA), 17 patients with oligodendroglioma (AO/AOD), and 190 grade IV glioblastoma (GBM).

Purpose/Objective: GBM is most common primary brain tumor and represents an important challenge for clinicians. These neoplasms are resistant to radio-chemotherapy. This might be explained by the fact that interactions between tumor and normal cells in tumor radioresistance through angiogenesis, hypoxia and immunosuppression, or an intrinsic radiosensitivity of cancer stem cells. A molecular analysis in tumor samples or peripheral blood of basal activation of different signaling pathways potentially involved in radioresistance could be of clinical interest. Phosphatidyl-inositol 3-kinase/protein kinase B (Akt) pathways serve to block apoptosis, keeping cells alive in very toxic environments such as chemotherapy and ionizing radiation. Polyclong group (PCG) proteins mediate gene silencing through histone post-translational modifications. PCg function is crucial for neural stem cell self-renewal. Recent evidence indicates that PCg genes are also required for cancer stem cell (CSC) propagation in neural tumors. In this study we evaluated the different genetic profile of Akt and EZH2 and clinical response to treatment in patient affected by GBM.

Materials and Methods: Our plan is to analyze fifty patients with GBM treated with Radio-chemotherapy (RT-CT) with temozolomide. Time to progression (TTP) after surgery or biopsy and overall survival (OS) will be used as clinical end-points to be correlated with polymorphisms of Akt and EZH2. DNA is extracted by proteinase K digestion. SNP genotyping was performed with the ABI PRISM 7900HT Sequence Detection System using primers and probes designed with Methyl Express software (v. 1.0). DNA samples (1-20 ng) from cancer tissue were amplified in multiplex Real-Time PCR. In addition, by quantifying them in a 25 fluorescent signals of the VIC and FAM probes, which specifically annealed to the biallelic sequences, the SDS software (v. 2.1) determined the allelic content of each sample.

Results: preliminary data is available for nineteen patients for polymorphisms of Akt after a follow-up of three- thirty-six months. The Akt1*3 wild-type genotypes was detected in 12/19 of samples and the heterozygous genotype was found in 7/19. We also evaluated Akt1*4 polymorphisms, and the only 2 patients that showed mutant genotypes had the longest survival time. The same analysis will be performed in peripheral blood in pts underwent to the same treatment for GBM, findings will be available for the ESTRO meeting in May.

Conclusions: This study is currently ongoing, we actively accruing new cases and we are waiting for the data of peripheral blood. This preliminary analysis appears to indicate allelic discrimination of SNPs cases and we are waiting for the data of peripheral blood. This retrospective analysis provides additional data out of a very limited number of studies about safety and feasibility of conventional 3D-conformal radiotherapy. The PFS is comparable to more complex and less abundant high-grade gliomas.

Materials and Methods: Patients with recurrence of malignant gliomas who failed after standard treatment of surgery, post operative radiotherapy (RT) and RT ± Temozolomide received bevacizumab (10 mg/kg i.v.) every two weeks until tumor progression and hypofractionation (16 x 2.66 Gy). The interval between the two radiotherapy treatments was at least 4 months in our patients. The median physical doses of the first and second radiation courses were 40-60 Gy and 40-60 Gy, respectively. The median cumulative biological equivalent doses (BED) were 215 Gy (α/β = 2 gy) and 100 Gy (α/β = 10 Gy): Median RT-volume was 143 cm³ and median cumulative RT-dose was 95 Gy. Results: 13 consecutive patients with recurrent malignant gliomas (6 GBM, 3 AAC, 3 LGG, 1 not applicable) received 2 cycles of bevacizumab prior to re-irradiation and underwent a repeat cranial radiosurgery. In this cohort and all patients responded to therapy. The median PFS after re-irradiation is 4.9 months, the median OS after re-irradiation is 8.2 months.

Conclusions: Conformal radiotherapy ± bevacizumab is save with a good quality of life for progressive HGG patients. These neoplasms are resistant to radiotherapy (temozolomide) does not increase neurotoxicity. The PFS is comparable to more complex and less abundant high-grade gliomas.