

## **STABILITY OF ACTIONABLE MUTATIONS IN PRIMARY AND RECURRENT GLIOBLASTOMAS**

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**INTRODUCTION:** Glioblastomas (GBMs) are the most common and aggressive subtype of glial brain tumor with a median survival of ~15 months. Current efforts to improve GBM patient survival are mostly based on a personalized medicine approach where individual patients are treated based on their acquired genetic changes. For ethical reasons, this approach is carried out at tumor recurrence. However, all molecular data is derived from the initial tumor: resections of recurrent GBMs are seldom performed. This study aims to assess whether genetic tumor changes of initial GBMs are still present at recurrence. This establishes whether repeated tumor biopsies are necessary prior to patient inclusion in targeted therapy trials for relapsing GBM.

**MATERIALS & METHODS:** DNA was isolated from pairs of initial and recurrent GBM (FFPE) tumor samples and subsequently sequenced on a panel of 365 oncogenes and tumor suppressor genes on the Illumina (next generation) sequencing platform. Mutation status was compared between primary and recurrent GBM samples and correlated with survival.

**RESULTS:** 129 patients were included in the analysis. Overall median survival was 20.8 months. Preliminary data showed that 6 out of 16 sequenced recurrent GBM samples (37.5%) either gained or lost point mutations in TP53, EGFR, PTEN, TERT, MTOR and MSH6 genes among others.

**DISCUSSION & CONCLUSION:** This preliminary data warrants caution when extrapolating genetic profiling data from initial to recurrent GBM tumors. A re-biopsy should be considered prior to treatment with targeted agents to characterize which causal genetic changes are retained and which are lost at tumor recurrence.

Keywords: Glioblastoma, GBM, Recurrent glioma, Genetics, NGS

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