ABSTRACT

J Neurooncol. 2022 Jan 8. doi: 10.1007/s11060-021-03917-1. Online ahead of print.

Impacts of genotypic variants on survival following reoperation for recurrent glioblastoma.

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INTRODUCTION: Recurrent glioblastoma (rGBM) prognosis is dismal. In the absence of effective adjuvant treatments for rGBM, re-resections remain prominent in our arsenal. This study evaluates the impact of reoperation on post-progression survival (PPS) considering rGBM genetic makeup.
METHODS: To assess the genetic heterogeneity and treatment-related changes (TRC) roles in re-operated or medically managed rGBMs, we compiled demographic, clinical, histopathological, and next-generation genetic sequencing (NGS) characteristics of these tumors from 01/2005 to 10/2019. Survival data and reoperation were analyzed using conventional and random survival forest analysis (RSF).
RESULTS: Patients harboring CDKN2A/B loss ($p = 0.017$) and KDR mutations ($p = 0.031$) had notably shorter survival. Reoperation or bevacizumab were associated with longer PPS (11.2 vs. 7.4-months, $p = 0.006$; 13.1 vs 6.2, $p < 0.001$). Reoperated patients were younger, had better performance status and greater initial resection. In 136/273 (49%) rGBMs undergoing re-operation, CDKN2A/B loss ($p = 0.03$) and KDR mutations ($p = 0.02$) were associated with shorter survival. In IDH-WT rGBMs with NGS data ($n = 166$), reoperation resulted in 7.0-month longer survival ($p = 0.004$) than those managed medically. This reoperation benefit was independently identified by RSF analysis. Stratification analysis revealed that EGFR-mutant, CDKN2A/B-mutant, NF1-WT, and TP53-WT rGBM IDH-WT subgroups benefit most from reoperation ($p = 0.03$). Lastly, whether or not TRC was prominent at re-operation does not have any significant impact on PPS (10.5 vs. 11.5-months, $p = 0.77$).
CONCLUSIONS: Maximal safe re-resection significantly lengthens PPS regardless of genetic makeup, but reoperations are especially beneficial for IDH-WT rGBMs with EGFR and CDKN2A/B mutations with TP53-WT, and NF1-WT. Histopathology at recurrence may be an imperfect gauge of disease severity at progression and the imaging progression may be more reflective of the prognosis.

DOI: 10.1007/s11060-021-03917-1
PMID: 34997451