Abstracts

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BIOM-31. TARGETED DNA SEQUENCING OF RECURRENT GlioBLASTOMA IDENTIFIES MOLECULAR FACTORS ASSOCIATED WITH CLINICAL OUTCOMES
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PURPOSE: The goal of our project was to define the molecular features of recurrent glioblastoma (rGBM) and their prognostic significance.

METHODS: We retrospectively reviewed 121 consecutive glioblastoma patients who underwent re-resection at a single institution from 2016-2021. Primary treatment in all patients included maximal safe resection followed by radiotherapy with concurrent and adjuvant temozolomide (TMZ). Capture-based targeted DNA sequencing for point mutations and copy number analysis was performed on all re-resection samples. Overall (OS) and progression-free survival (PFS) from re-resection were analyzed with the Kaplan-Meier method and Cox regression analyses. RESULTS: Median age at first recurrence was 57 years (range, 27-78) and follow up from re-resection was 11 months. Salvage therapy comprised re-irradiation (n = 52, 43%), temozolomide (TMZ) (n = 39, 32%), lomustine (n = 47, 39%), and/or bevacizumab (n = 22, 18%). Median OS and PFS were 12.1 and 4.4 months, respectively. Median tumor mutation burden (TMB) was 4 mut/Mb (range, 1-650), average unstable microsatellite sites (MSI) were 1.16% (range, 0-20), and MGMT promoter methylated in 71 (59%) patients. Longer OS was found after postoperative TMZ (19.3 vs. 9.1), KPS > 70 (13.6 vs. 11.1), and/or re-irradiation (12.6 vs. 8.4) (p< .05). On multivariate analysis, TMZ (HR 0.2, 0.079-0.48), re-irradiation (HR 0.27, 0.12-0.58), and mutations in PDGFRA (HR 0.24, 0.067-0.83) or PTEN (HR 2.3, 1.1-4.8) genes were associated with longer OS after re-resection (p< .05). Multivariate predictors of re-irradiation response included MSI >1.16 (HR 0.25, 0.084-0.75), and mutations in PDGFRA (HR 0.04, 0.005-0.33), TERT (HR 0.16, 0.033-0.78), or PIK3R1 (HR 0.18, 0.041-0.8) genes. In the 46 matched primary/recurrent tumors, 40 (87%) had a change in a mutation and 9 (20%) demonstrated hypermutation, of which 4 (44%) had mismatch repair deficiencies. CONCLUSIONS: Our study outlines the molecular factors associated with survival and response to re-irradiation in rGBM as well as the molecular differences between primary/recurrent samples.