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Clinical and Genetic Markers of Vascular Toxicity in Glioblastoma Patients: Insights from NRG Oncology RTOG-0825

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Abstract

Background: Glioblastoma (GBM) is an aggressive form of brain cancer in which treatment is associated with toxicities that can result in therapy discontinuation or death. This analysis investigated clinical and genetic markers of vascular toxicities in GBM patients during active treatment.

Methods: 591 Non-Hispanic White GBM patients with clinical data were included in the analysis from NRG RTOG-0825. Genome-wide association studies (GWAS) were performed from genotyped blood samples (N=367) by occurrence of thrombosis or hypertension (grade ≥2). A clinical prediction model was produced for each vascular toxicity. Significant GWAS variants were then added to the clinical model as a single nucleotide polymorphism (SNP) -dose effect variable to produce the final genetic models.

Results: Thrombosis and hypertension were experienced by 62 (11%) and 59 (10%) patients, respectively. Patients who experienced hypertension displayed improved survival over those without hypertension (median overall survival: 25.72 vs 15.47 months, p=0.002). The genetic model of thrombosis included corticosteroid use (OR: 7.13, p=0.02), absolute neutrophil count (OR: 1.008, p=0.19), body surface area (OR: 18.87, p=0.0008), and the SNP-dose effect (3 variants; OR: 3.79, p<.0001). The genetic model of hypertension included bevacizumab use (OR: 0.97, p=0.95) and the SNP-dose effect (6 variants; OR: 4.44, p<.0001).

Conclusion: In this study, germline variants were superior in predicting hypertension than clinical variables alone. Additionally, corticosteroid use was a considerable risk factor for thrombosis. Future investigations should confirm the hazard of corticosteroid use on thrombosis and the impact of bevacizumab in other malignancies after accounting for the genetic risk of hypertension.

Keywords: bevacizumab; genome-wide association study; glioblastoma; hypertension; thrombosis.