

## ABSTRACT

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Bevacizumab plus irinotecan with or without gamma knife radiosurgery after failure of concurrent chemo-radiotherapy for high-grade glioma.

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**INTRODUCTION:** Concurrent chemo-radiotherapy (CCRT) with temozolomide (TMZ) is a standard first-line treatment for high-grade glioma. However, if CCRT with TMZ treatment fails, second-line treatment options have limited value. Bevacizumab plus irinotecan is the only available treatment option for such patients. The role of gamma knife radiosurgery (GKS) in patients with high-grade gliomas is not well-established. In this study, we evaluated the efficacy and safety of bevacizumab plus irinotecan with or without GKS in the treatment of high-grade glioma patients who progressed after initially being treated with CCRT with TMZ.

**METHODS:** We collected clinical data of patients with biopsy-proven high-grade glioma (glioblastoma multiforme (GBM) or anaplastic astrocytoma) who were treated at Samsung Medical Center from January 2015 to December 2020, retrospectively. We evaluated the overall survival (OS), progression-free survival (PFS), and safety of bevacizumab plus irinotecan with or without GKS.

**RESULTS:** In total, 203 patients were diagnosed with high-grade glioma, including GBM and anaplastic astrocytoma. The median OS was 8.73 months (95% confidence interval [CI]: 7.27-10.18), and the median PFS was 4.36 months (95% CI: 3.75-4.97). Sixty-eight (33.4%) patients underwent GKS prior to bevacizumab plus irinotecan treatment, which led to a significantly prolonged OS (10.13 months, 95% CI: 8.65-11.60 vs. 8.26 months, 95% CI: 7.01-9.51,  $p = 0.012$ ). The most common adverse events of any grade were neutropenia (36.9%) and thrombocytopenia (22.6%). However, the incidence of adverse events in patients who underwent GKS prior to bevacizumab plus irinotecan was not different compared with those in patients who did not undergo GKS.

**CONCLUSIONS:** Bevacizumab plus irinotecan was well-tolerated and moderately effective in patients with high-grade gliomas. The addition of GKS prior to bevacizumab plus irinotecan led to a significant OS benefit with a manageable safety profile. GKS prior to bevacizumab plus irinotecan can therefore be considered a potential treatment option for these patients.

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