## ABSTRACT

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Boron neutron capture therapy and add-on bevacizumab in patients with recurrent malignant glioma.

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BACKGROUND: Although boron neutron capture therapy has shown excellent survival data, previous studies have shown an increase in radiation necrosis against recurrent malignant glioma. Herein, we proposed that bevacizumab may reduce radiation injury from boron neutron capture therapy by re-irradiation. We evaluated the efficacy and safety of a boron neutron capture therapy and add-on bevacizumab combination therapy in patients with recurrent malignant glioma.

METHODS: Patients with recurrent malignant glioma were treated with reactor-based boron neutron capture therapy. Treatment with bevacizumab (10 mg/kg) was initiated 1-4 weeks after boron neutron capture therapy and was administered every 2-3 weeks until disease progression. Initially diagnosed glioblastomas were categorized as primary glioblastoma, whereas other forms of malignant glioma were categorized as non-primary glioblastoma.

RESULTS: Twenty-five patients (14 with primary glioblastoma and 11 with non-primary glioblastoma) were treated with boron neutron capture therapy and add-on bevacizumab. The 1-year survival rate for primary glioblastoma and non-primary glioblastoma was 63.5% (95% confidence interval: 33.1-83.0) and 81.8% (95% confidence interval: 44.7-95.1), respectively. The median overall survival was 21.4 months (95% confidence interval: 7.0-36.7) and 73.6 months (95% confidence interval: 11.4-77.2) for primary glioblastoma and non-primary glioblastoma, respectively. The median progression-free survival was 8.3 months (95% confidence interval: 4.2-12.1) and 15.6 months (95% confidence interval: 3.1-29.8) for primary glioblastoma and non-primary glioblastoma, respectively. Neither pseudoprogression nor radiation necrosis were identified during bevacizumab treatment. Alopecia occurred in all patients. Six patients experienced adverse events ≥grade 3.

CONCLUSIONS: Boron neutron capture therapy and add-on bevacizumab provided a long overall survival and a long progression-free survival in recurrent malignant glioma compared with previous studies on boron neutron capture therapy alone. The add-on bevacizumab may reduce the detrimental effects of boron neutron capture therapy, including pseudoprogression and radiation necrosis. Further studies of the combination therapy with a larger sample size and a randomized controlled design are warranted.

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