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Levels of circulating endothelial cells in relapsing glioblastoma patients responding to bevacizumab.

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Abstract

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Background: Bevacizumab, an anti-VEGF antibody, is active in a fraction of high-grade gliomas. Circulating endothelial and progenitor cells (CECs and CEPs, respectively), contribute to the formation of tumor vessels and their number may correlate with the degree of tumor angiogenesis.

Methods: We tested this relationship in 24 patients with recurrent, high-grade gliomas (19 glioblastomas, GBM; 5 anaplastic astrocytomas, AA) treated with bevacizumab (10 mg/kg every two weeks) and Irinotecan (125 mg/m² every two weeks for patients not on EIAEDs and 340 mg/mq for patients on EIAEDs) after approval of the Ethical Committee of the Neurological Institute C. Besta. The number and viability of CECs and CEPs were measured before treatment and every 2 months by six color cytometry. CECs were enumerated as Syto+CD45- CD31+/P1h12+ cells, CEPs as Syto+CD45- CD31+/CD133+ cells; CEC subpopulations expressing CD109 were also enumerated.

Results: Median age was 53 years (range 15-66), median Karnofsky Performance Status (KPS) 70 (range 50-100), median number of prior chemotherapies 2 (range 1 to 4), median follow-up 5.5 months. Five patients had progressive disease at first MRI; 14 patients achieved partial response, 4 stable disease and one was lost to follow-up. Overall, 6M-PFS was 50% and 6M-OS 63%. Median PFS and OS were 6 and 10 months, respectively. For GBM, 6M-PFS was 47% and 6M-OS 68%. At baseline the number of CECs was significantly higher in GBM than in AA (123.4 ± 50.7 vs. 61 ± 31, p = 0.009). A significant reduction of CECs and viable CECs was only observed in GBM with a clinical and radiologic response after two months of therapy (CECs 121.6 ± 54.4 vs. 80.9 ± 60.3, p=0.05; viable CECs 33.4 ± 18.3 vs. 16.2 ± 16.4, p = 0.03). Higher levels of CD109+ CECs at baseline were observed in patients who achieved a treatment response lasting at least 4 months.

Conclusions: The data encourage the investigation of the predictive value of viable CECs on a larger number of GBM treated by bevacizumab.

Author Disclosure

Employment or Leadership Position	Consultant or Advisory Role	Stock Ownership	Honoraria	Research Funding	Expert Testimony	Other Remuneration
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