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Prospective evaluation of angiogenic, hypoxic and EGFR-related biomarkers in recurrent glioblastoma multiforme treated with cetuximab, bevacizumab and irinotecan.

Hasselbalch B, Eriksen JG, Broholm H, Christensen IJ, Grunnet K, Horsman MR, Poulsen HS, Stockhausen MT, Lassen U.

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Abstract

Hasselbalch B, Eriksen JG, Broholm H, Christensen IJ, Grunnet K, Horsman MR, Poulsen HS, Stockhausen M-T, Lassen U. Prospective evaluation of angiogenic, hypoxic and EGFR-related biomarkers in recurrent glioblastoma multiforme treated with cetuximab, bevacizumab and irinotecan. *APMIS* 2010; 118: 585-94. Several recent studies have demonstrated a beneficial effect of anti-angiogenic treatment with the vascular endothelial growth factor-neutralizing antibody bevacizumab in recurrent high-grade glioma. In the current study, immunohistochemical evaluation of biomarkers involved in angiogenesis, hypoxia and mediators of the epidermal growth factor receptor (EGFR) pathway were investigated. Tumor tissue was obtained from a previous phase II study, treating recurrent primary glioblastoma multiforme (GBM) patients with the EGFR inhibitor cetuximab in combination with bevacizumab and irinotecan. Of the 37 patients with available tumor tissue, 29 were evaluable for response. We concurrently performed immunohistochemical stainings on tumor tissue from 21 GBM patients treated with bevacizumab and irinotecan. We found a tendency of correlation between the hypoxia-related markers, indicating that they share the same regulatory mechanisms. None of the EGFR-related biomarkers showed any significant correlations with each other. None of the biomarkers tested alone or in combination could identify a patient population likely to benefit from bevacizumab and irinotecan, with or without the addition of cetuximab. There is still an urgent need for one or more reliable and reproducible biomarkers able to predict the efficacy of anti-angiogenic therapy.

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