Angiogenesis inhibitors in tackling recurrent glioblastoma

Thomas Hundsberger, David A Reardon & Patrick Y Wen

INTRODUCTION
Despite aggressive multimodality treatment of glioblastoma, outcome remains poor and patients mostly die of local recurrences. Besides reoperation and occasionally reirradiation, systemic treatment of recurrent glioblastoma consists of alkylating chemotherapy (lomustine, temozolomide), bevacizumab and combinations thereof. Unfortunately, antiangiogenic agents failed to improve survival either as a monotherapy or in combination treatments. This review provides current insights into tumor-derived escape mechanisms and other areas of treatment failure of antiangiogenic agents in glioblastoma. Areas covered: We summarize the current literature on antiangiogenic agents in the treatment of glioblastoma, with a focus on recurrent disease. A literature search was performed using the terms "glioblastoma", "bevacizumab", "antiangiogenic", "angiogenesis", "resistance", radiotherapy", "chemotherapy" and derivations thereof. Expert commentary: New insights in glioma neoangiogenesis, increasing understanding of vascular pathway escape mechanisms, and upcoming immunotherapy approaches might revitalize the therapeutic potential of antiangiogenic agents against glioblastoma, although with a different treatment intention. The combination of antiangiogenic approaches with or without radiotherapy might still hold promise to complement the therapeutic armamentarium of fighting glioblastoma.