EDITORIAL

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Reconsidering Low-Dose Bevacizumab Regimens in High-Grade Gliomas: A Policy Brief for Resource-Limited Settings

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Dear Editor

High-grade gliomas, particularly glioblastoma, represent some of the most aggressive primary tumors of the central nervous system. Despite standard treatment approaches including surgery, radiotherapy, and temozolomide-based chemotherapy, the prognosis remains poor with early recurrence [1, 2]. A hallmark pathological feature of these tumors is profound angiogenesis driven by overactivation of the vascular endothelial growth factor (VEGF) pathway [3]. In this context, bevacizumab, a monoclonal antibody targeting VEGF, has gained a notable role in the management of high-grade gliomas, especially in the recurrent setting [4, 5]. Although bevacizumab has failed to show a consistent benefit in overall survival in randomized trials, it has shown improvements in progression-free survival, radiographic response rates, reduction in cerebral edema, corticosteroid dependence, and quality of life [6-8]. Hence, it is still widely used as a second-line or salvage therapy in recurrent high-grade gliomas.

Given its widespread use in this context, questions regarding the optimal dosing strategy have become increasingly relevant. The conventional dose of bevacizumab in glioblastoma (10 mg/kg every two weeks) has been largely extrapolated from the treatment regimens of other solid malignancies [9]. Nonetheless, this dosing regimen was not particularly designed for central nervous system malignancies. To date, there is no conclusive evidence that supports the superiority of the standard dose over the lower-dose regimens in glioblastoma [10]. In recent years, retrospective studies and phase II trials have indicated that the lower doses of bevacizumab, including the 5 mg/kg dose, may provide comparable efficacy in terms of progression-free survival and even overall survival [11, 12]. From a biological perspective, the vascular normalization hypothesis offers a credible explanation for dose optimization. Overly aggressive blockade of VEGF could result in over-pruning of the tumor vasculature, hypoxia, and impaired delivery of concurrent therapies. On the other hand, partial blockade of VEGF could induce a transient normalization of the abnormal tumor vasculature, resulting in a more organized and functional network [12]. This concept supports the possibility that lower-dose regimens may achieve sufficient biological effect while minimizing toxicity.

Bevacizumab is usually used in combination with temozolomide, irinotecan, CCNU (lomustine), carboplatin, and other chemotherapeutic drugs [8, 13, 14]. In randomized clinical trials assessing the treatment modalities for glioblastoma, the role of new drugs, including immunotherapeutic agents, has failed to show a significant benefit in overall survival [15]. In this context, the role of bevacizumab is best defined in symptom management, alleviation of cerebral edema, and reduction of corticosteroid dependence [16, 17]. The lower doses of bevacizumab regimens, especially in association with lower doses of corticosteroids, may offer similar benefits in symptom control and disease stabilization with potential decreased toxicity and cost.

In resource-limited settings, financial constraints remain a major barrier to optimal cancer treatment, particularly for expensive biologic and targeted therapies. Systematic reviews and meta-analyses have demonstrated that financial toxicity is highly prevalent among patients with cancer in low- and middle-income countries, where out-of-pocket expenditures can significantly affect treatment adherence and outcomes [18, 19]. Global analyses have further highlighted substantial disparities in the affordability and access to anticancer medicines between high-income and low-income countries [20]. In the era of molecularly targeted agents and immunotherapies, the economic burden of cancer care has intensified, increasing the risk of treatment interruption or abandonment [18]. Moreover, extensive literature reviews have also validated the fact that the issues of accessibility, affordability, and pricing of anti-cancer drugs are still major challenges in the current healthcare settings [21]. In this context, treatment modalities that take into account dose optimization, provided they are evidence-based, may be a sensible approach to enhance accessibility.

In conclusion, reconsideration of the standard bevacizumab dosing strategy in high-grade gliomas is supported by emerging clinical evidence and biological rationale. Lower-dose bevacizumab regimens may potentially offer similar levels of disease control with improved safety profiles and cost-effectiveness. In the absence of conclusive evidence supporting the use of higher doses of bevacizumab, prospective randomized studies are urgently required to compare the standard versus reduced doses of bevacizumab.

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