Bevacizumab as Second-line Treatment of Glioblastoma – Worth the Effort?

Role bevacizumabu ve druhé linii léčby glioblastomu – zmařené naděje?

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Summary

Objective: To evaluate the role of bevacizumab and irinotecan as second-line treatment of glioblastoma in patients with progression after radiotherapy and temozolomide. ***Methods:*** A retrospective analysis of 16 subjects was performed with overall survival and toxicity evaluation as the primary endpoint. ***Results:*** The analysis revealed serious toxicity of this highly expensive regimen without proving an improvement in overall survival of patients in comparison to a control group. ***Conclusion:*** Unless there are robust data from phase III clinical trials, including quality of life assessments or evaluation of predictive biomarkers to guide therapy, bevacizumab and irinotecan regimen should be spared for cautiously selected patients, especially in countries with limited budget for oncological treatment.

Key words

glioblastoma multiforme – treatment – targeted agents – bevacizumab – overall survival

Souhrn

Cíl: Posouzení role bevacizumabu a irinotekanu v druhé linii léčby glioblastomu u pacientů s progresí nemoci po radioterapii a temozolomidu. ***Metody:*** Retrospektivní analýzou bylo hodnoceno celkové přežití a toxicita léčby u 16 pacientů. ***Výsledky:*** Byla zaznamenána vysoká toxicita této ekonomicky náročné léčby, bez průkazu prodloužení celkového přežití. ***Závěr:*** Bez přesvědčivých dat z klinických studií třetí fáze, včetně posouzení kvality života a případných prediktivních markerů, by kombinovaná léčba bevacizumabem a irinotekanem měla být v krajinách s omezeným léčebným rozpočtem používána s opatrností a pouze u vybraných pacientů.

Klíčová slova

multiformní glioblastom – léčba – cílená léčba – bevacizumab – celkové přežití

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Autoři deklarují, že v souvislosti s předmětem studie nemají žádné komerční zájmy.

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Glioblastoma multiforme is one of the most aggressive human cancers, associated with significant neurological morbidity and very poor survival rates [1].

It was almost a decade ago when temozolomide combined with radiotherapy, became established as a standard of care for patients who underwent a surgery for glioblastoma [2], yielding a two-month increase in overall survival compared to radiotherapy alone.

Latest phase II studies with bevacizumab as a single agent or in combination therapy with cytotoxic agents such as irinotecan in patients with grade 3 and grade 4 malignant gliomas [3,4] demonstrated a significant clinical response, leading to its subsequent approval by the FDA [5].

A total of 16 patients from our oncologic unit, with a histologically documented grade 4 glioblastoma multiforme were evaluated. All of them received temozolomide as first-line treatment in combination with radiotherapy, and subsequently experienced disease progression to an unresectable stage, considered either as radiological progression or clinical status deterioration. The median age was 62 (ranging from 43 to 78 years of age) and these patients were eligible for further therapy with irinotecan and bevacizumab. The median number of administered treatment cycles was 7 (ranging from 2 to 12) and the median overall survival of patients receiving a second-line treatment was 5.2 months (from 0.8 to 9 months), without any significant difference in comparison to patients receiving best supportive care [6]. The toxicity of this treatment in this particular subset of generally very ill patients is also a matter of concern. Among the main adverse events we noted three intracranial haemorrhages, four cases of newly diagnosed severe hypertension and two bowel perforations. The overall cost of managing adverse effects of the treatment were relatively high, not to mention the drug's high price.

Other trials involving other VEGF inhibitors have also failed to prove its benefits in this type of tumour [7], some of them suggesting lomustine as a control arm in future post temozolomide progression trials [7].

We are aware of the fact that the study population of our retrospective analysis is too small to draw conclusions concerning the adoption of a certain regimen as a standard of treatment, yet, it provides a reference that should not be neglected.

We strongly believe that, at least while there are no robust phase III trials with quality of life assessments, since we unfortunately do not have any predictive biomarker to guide therapy, the bevacizumab + irinotecan scheme should be very carefully used, if ever, in well selected patients, especially in limited cancer budget countries.

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