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### **Reply to Letter to the Editor**

## Role of surgery for glioblastoma: response to letters from Dr. Gerritsen and his colleagues and Dr. Vargas Lopez

We thank Dr. Gerritsen and his colleagues and Dr. Vargas Lopez for their comments regarding the role of surgery for patients with glioblastoma, with reference to our consensus review article appearing in this journal.<sup>1</sup>

We agree with Dr. Gerritsen and his colleagues regarding the importance of maximizing the extent of resection while minimizing the risk of neurological morbidity. They propose a novel grading scale to translate these surgical goals into a merged "onco-functional clinical outcome." Such an instrument combining assessment of the extent of resection with one evaluating functional outcome or both quality of life and neurologic function would potentially be an important contribution but would need further prospective evaluation.

We agree with Dr. Vargas Lopez that salvage surgery is an important treatment option to consider for subsets of glioblastoma patients, especially those with large symptomatic lesions. However, we interpret the limited data to indicate that only patients who undergo gross total tumor resections are likely to derive a survival benefit.<sup>2,3</sup> If only a subtotal reaction is possible, a reoperation is unlikely to benefit the patient in terms of improving survival. As Dr. Vargas Lopez indicates, there are retrospective series and meta-analyses suggesting potential benefit of surgery, but these all have limitations, including selection bias, and represent low-level evidence data. Despite the importance of this issue, randomized controlled studies or other high-quality studies to guide our practice have been very challenging to perform. We had also already indicated that the level of evidence for all other interventions, not only surgery, is low.

As Dr. Vargas Lopez indicates, bevacizumab may affect wound healing and increase the risk of reoperation. If a patient requires surgery, then bevacizumab should indeed be withheld. However, for many patients who do not necessarily require immediate surgery, the rationale of holding bevacizumab to keep open the option of surgery could also deprive the patient of a treatment that could potentially improve their quality of life.

Whether a patient undergoes a reoperation requires careful balancing of the potential risks and benefits, taking into account the tumor location, the extent of resection possible, need for tissue to guide treatment decision, the patient's condition, prognosis and preference, and the availability of further therapy following surgery. It is a useful treatment option for many patients, but sometimes is also used excessively and inappropriately and needs to be considered in the context of the other available treatments. Multidisciplinary consensus is likely to serve the patient's interest best in this setting. In the future, reoperation may play a greater role in the treatment of patients with recurrent glioblastomas as part of "window-ofopportunity" and "neoadjuvant" surgical trials, to administer novel therapies with poor penetration across the blood-brain barrier, or potentially to obtain tissue for analysis to guide further therapy.

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