Abstract

A novel highly sensitive VEGF-responsive reporter gene assay has been developed that allows bevacizumab activity to be quantified rapidly and in a highly specific manner. The use of this assay has shown that in a cohort of patients with glioblastoma who respond to therapy there is a close correlation between bevacizumab drug levels determined by ELISA and bevacizumab activity determined using the VEGF-responsive reporter gene assay. In contrast, in secondary non-responders with a decreasing PK profile, bevacizumab drug levels determined by ELISA are consistently higher than bevacizumab activity determined using the reporter gene assay, suggesting that bevacizumab activity is partially neutralized by anti-drug neutralizing antibodies (NAbs). The results obtained suggest that the use of the VEGF-responsive reporter gene assay may allow the appearance of anti-bevacizumab NAbs to be used as a surrogate maker of treatment failure prior to the clinical signs of disease progression.

Conclusion

A good correlation between bevacizumab drug levels determined by ELISA and bevacizumab activity determined using a VEGF-responsive reporter gene assay was observed in patients with glioblastoma who respond to therapy. In contrast, in secondary non-responders with a decreasing PK profile bevacizumab drug levels determined by ELISA are similar or higher than bevacizumab activity suggesting that bevacizumab activity is partially neutralized by anti-drug neutralizing antibodies (NAbs). Additional studies are necessary in order to determine whether the use of the VEGF-responsive reporter gene assay will provide a means of detecting the early appearance of anti-bevacizumab NAbs as a surrogate maker of treatment failure.

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