Nivolumab and Bevacizumab for recurrent Glioblastoma; A Translational Trial in Progress

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Glioblastoma multiforme (GBM) is the most common and aggressive adult brain tumor. Regardless of improved treatment over the last 10 years the prognosis remains poor. Current standard of care at diagnosis is surgical resection, followed by radiotherapy and temozolomide. Receiving this therapy the 2 – and 5-year overall survivals are 27.2% and 9.8%, respectively [1] and the median survival is 14.6 months [2]. We have no standard treatment for relapse and known options have limited effect. Therefore, there is an urgent need for novel treatment interventions to improve clinical outcomes and quality of life for these patients. There has recently been shown benefits in overall survival achieved with immunotherapeutics in melanoma, non-small cell lung cancer (NSCLC) and renal cell carcinoma. Accordingly, it has been posited that immunotherapy may also offer promise in other difficult cancers such as GBM [3].

We present our translational study; a phase II open label, two-armed translational study of Nivolumab and Bevacizumab for recurrent GBM, who have failed prior treatment with radiation and temozolomide. The patients are included in either two arms depending on possibly salvage neurosurgical resection. Both arms receive Nivolumab combined with Bevacizumab administrated every second week. We expect 40 patients; 20 in each arm, and the enrollment period is expected to 20 months and started October 2018. The primary objective is to make preliminary assessment of PD-L1 and other immune related biomarkers that might act as predictors of antitumor activity of Nivolumab, therefore we perform full genome sequencing on the tumor biopsy and on blood samples from both patient groups. Changes in the transcriptomic landscape caused by check-point inhibition and relation to response as compared with baseline sequencing data. In addition, we investigate the impact of high TMB and neoepitope load. To investigate the tumor microenvironment, we harvest tumor infiltrating lymphocytes on fresh biopsies from patients undergoing surgical resection and study the composition by flow-cytometry. The patients are evaluated by blood samples, FET-PET as wells as clinical and neurological examinations to evaluated PFS and OS. Overall, the study will provide us with a unique possibility to investigate which patients will profit from the treatment.

Reference list

1. Stupp R et al.: Lancet Oncol 2009, 10(5): 459-466.
2. Stupp R, et al.: N Engl J Med 2005, 352: 987-996.
3. Heimberger AB, et al..: Neuro Oncol 2011, 13: 3-13.

May 2021