Survival and T-cell tumor reactivity in patients treated with nivolumab and bevacizumab for recurrent glioblastoma in the clinical trial CA209-9UP, Abstract, EANO, September 2022.

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Background:

Glioblastoma (GBM) is an aggressive brain tumor with a median survival of 14.6 months. We have no standard treatment for relapse and current treatment options have limited effect. Novel treatments are necessary to improve survival and quality of life.

Material and Methods:

We present data from; a phase II open label, two-armed clinical trial studying nivolumab and bevacizumab in treatment of recurrent GBM, with progression after Stupp's regime. Patients were included in two arms depending on the possibility of salvage neurosurgical resection. All patients had biopsies for genome sequencing at primary tumor and recurrence. Both arms received nivolumab and bevacizumab administrated every second week and the surgical arm also received neoadjuvant nivolumab 7 days prior to surgery. Fresh tissue samples were collected for tumor digest, TILs (tumor infiltrating lymphocytes) for phenotype exploration and intracellular staining to test reactivity. Patients were treated until progression, death, or intolerable side effects. Toxicity screens were reported, and follow-up ended in Marts 2022.

Results:

Forty-four patients were included from November 2018 to January 2022; 20 in each arm (four screen-failures). Treatment was overall well tolerated. Median (m) age at inclusion was 57,5 years (arm A) and 50,5 years (arm B), and the groups had an even distribution. The surgical and non-surgical arm had an mPFS of 5.95 and 3.83 months respectively, while the mOS was 13.96 months and 6.77 months, respectively. Multivariate analysis was performed by variables such us steroid, MGMT, gender, age at diagnosis, resection extent and arm. Steroid at inclusion was a significant negative predictor of outcome ($p = 0.0378$). Controls from our GBM registry (N=140), which were treated with neurosurgical resection and then bevazicumab and irinotecan in recurrent setting had an mOS of 8.64 months (log-rank $p=0.0181$).

Furthermore, reactive tumor infiltrating lymphocytes (TIL) were detected in four of the patients who presented with a longer mOS and mPFS of 16.75 months and 9.18 months, while the 16 patients without TIL reactivity had mOS and mPFS of 12.63 months and 5.13 months, respectively (not significant).

Conclusions:

We found an increased mOS in patients treated with nivolumab and bevacizumab at recurrence, compared to our controls: 13.96 months and 8.64 months, respectively. Four patients with T-cell reactivity towards tumor cells showed an even longer mPFS and mOS. Though not significant, these results warrant further research evaluation in larger patient cohorts. We are currently investigating proteomics and sequencing data to identify predictive biomarkers.

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