

B3

Title: CITE-seq Identifies increased immune activation in patients treated with Nivolumab and Bevacizumab in Randomized Phase 2 Study in Recurrent Glioblastoma (rGBM)

Author(s): Vineeth Tatineni, Tyler J Alban, Matthew Grabowski, Balint Otvos, Defne Bayik, Pat Raymond, C. Marcela Diaz-Montero, , Justin D Lathia, Manmeet S Ahluwalia

Affiliation: Cleveland Clinic

Glioblastoma (GBM) creates an immunosuppressive environment that presents a challenge to the efficacy of immunotherapeutic approaches aimed at increasing T cell activation by immune checkpoint inhibition. Results from the CheckMate-143 trial demonstrated responses in 8% of patients treated with Nivolumab, underscoring the need for further insight into the mechanisms and markers of immune suppression and response. Here we analyzed patient's peripheral blood samples in a randomized, phase 2 study of Nivolumab and bevacizumab standard vs low dose, at GBM first recurrence (NCT03452579). In this study we identified 8 responders and 8 non-responders at 8 weeks post treatment as well as 4 bevacizumab only treated patients as controls, and performed 10X Genomics simultaneous cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq) to understand how their immune system was differentially changing during treatment. Analysis was performed comparing responders and non-responders as well as bevacizumab dosing cohorts to help understand how it might be playing a role with Nivolumab treatment. Initial analyses did not reveal any differences in peripheral immune populations between responders and non-responders post treatment, however standard dose bevacizumab treated patients had a significant reduction in MDSCs post treatment. Furthermore, the gene expression profile of total immune populations revealed an immune activated state in the standard dose treated cohort, which was not observed in the low dose bevacizumab group. Importantly, standard bevacizumab treated patients tended to have increased response to therapy. Ongoing analysis includes comparison on bevacizumab only treated patients to the Nivolumab + bevacizumab treated groups to help identify the individual and combined effects.