

### C3

#### **Title: Randomized Phase 2 Study of Nivolumab (nivo) plus Either Standard or Reduced Dose Bevacizumab (bev) in Recurrent Glioblastoma (rGBM)**

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**Background:** Trials with anti-PD1 in rGBM have shown limited efficacy. VEGF is highly upregulated proangiogenic growth factor in GBM contributing to tumor-associated immunosuppression. Preclinical data suggests a potential dose effect of anti-VEGF therapy on immunomodulation. Hence, a combination of anti-PD1 and anti-VEGF may be a promising approach in rGBM.

**Methods:** 90 patients with first-recurrent GBM were randomized(1:1) to nivolumab (240 mg IV Q2 weeks) and bevacizumab at standard (10 mg/kg; Arm A) or low dose (3 mg/kg; Arm B) IV Q2 weeks. Eligibility also required KPS  $\geq$  70% and dexamethasone  $\leq$  4 mg/day. Stratification included extent of resection, age, performance status and MGMT methylation status. Single cell RNA sequencing with CITE-seq was used to analyze blood samples from pre- and 8 weeks post-treatment among 8 responders and 8 non-responders.

**Results:** 90 patients were enrolled (May 2018- Jan 2020) and median follow-up is 5.5 months. Characteristics in 2 arms were comparable. Median age was 60.5 years (range 27-86), median KPS was 80. 35 patients were MGMT methylated, 53 unmethylated and 2 indeterminate. Estimated progression free survival (PFS) and median overall survival (OS) in arm A are 6.13 and 10.85 months and 4.59 and 9.61 months in Arm B, respectively for 16 patients underwent including 8 responders and 8 non-responders. Cohort A patients had decreased myeloid derived suppressor cells and an inflammatory response gene signature by CITE-seq. Most frequent toxicities included fatigue (51%), headache (31%), diarrhea (30%) and hypertension (23%). Toxicity was comparable between 2 arms, except hypertension was more common in arm A.

**Conclusions:** PFS and OS rates appear similar for nivolumab with either standard or low-dose bevacizumab. Ongoing response evaluation and immunocorrelative data will be presented.