EXTH-76. THE INOVIVO SYSTEM: A NOVEL PRECLINICAL TOOL FOR IN VIVO DELIVERY OF TUMOR TREATING FIELDS (TTFIELDS)

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Massachusetts; Department of Neurosurgery, - , Rohinton S., Alexander 2, 1 Massachusetts General Hospital and - , Gina , Daniel cm/s, cm/s. The efflux ratio values were 0.46–0.79 for , 14 -C]-ONC201 material DISTRIBUTION IN THE CENTRAL NERVOUS SYSTEM EXTH-77. ONC201 EXHIBITS PASSIVE DIFFUSION AND BROAD TUMOR TREATING FIELDS (TTFIELDS) EXTH-76. THE INOVIVO SYSTEM: A NOVEL PRECLINICAL TOOL FOR IN VIVO DELIVERY OF TUMOR TREATING FIELDS (TTFIELDS) Immune checkpoint inhibitors (ICI) have revolutionized oncologic treatment for metastatic melanoma. With improved systemic control, there has been increasing prevalence of patients with brain metastases. Recent evidence has demonstrated intracranial responses in a subset of these patients treated with ICI. We hypothesize that the response to ICI in melanoma brain metastases (MBM) is reflective of unique features within the tumor microenvironment of the brain. A cohort of 27 patients, encompassing 8 pre- and 19 post-immunotherapy MBM underwent single cell RNA sequencing (Smart-Seq2). The cohort includes patients with longitudinal cranial resections and simultaneously resected, spatially distinct tumors. Each tumor underwent unsupervised transcriptomic analysis, differential gene expression, infered copy number variation, and T-cell receptor (TCR) clonotyping. Published extracranial melanoma single cell datasets were used to compare the tumor microenvironment of the brain and periphery in response to ICI. A total of 14,027 cells (6,189 malignant, 7,838 non-malignant) were sequenced. Brain metastases demonstrated a heterogeneous distribution of macrophage states. Intracranial macrophages were found to be more tumor-supportive than their extracranial counterparts. MBM also included a distribution of reactive neutrophils and astrocytes. Analysis across pre- and post-treatment MBM demonstrated an increase in clonally expanded T cells in patients responding to ICI. Across longitudinal brain metastases collected from the same patients, there was evidence of identical T cell clones across timepoints and locations. Single cell sequencing of MBM provides insights into the cellular composition of the tumor and microenvironment. Our data suggest the cellular heterogeneity within MBM is unique when compared to extracranial disease. Additionally, T cell clonal expansion is found following ICI and T cells of the same clonotype infiltrate spatially and temporally separated brain metastases. These findings raise potential therapeutic implications as we learn to target the different features of the innate and adaptive immune system within brain metastases and their extracranial counterparts.

IMMU-02. THE SURVIVAL OUTCOMES ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS FOR NON-SMALL CELL LUNG CARCINOMA PATIENTS WITH BRAIN METASTASES IN THE UNITED STATES Nayan Lamba, 1 Timothy Smith, 2 and Ryan Forgues 3; 1 Massachusetts General Hospital, Boston, MA, USA, 2 Department of Neurosurgery, Brigham and Women’s Hospital, Boston, MA, USA, 3 Brigham and Women’s Hospital, Boston, MA, USA BACKGROUND: Management of advanced NSCLC has been transformed by PD-1/PD-L1 immune checkpoint inhibitors (ICI), with FDA approvals in 2015 (second-line) and 2016 (first-line). Because patients with