IMPS-26. HARNESSING THE MYELOID CHECKPOINT CD47-SIRPa AXIS AGAINST ADULT AND PEDIATRIC MALIGNANT BRAIN TUMORS: A NOVEL IMMUNOTHERAPEUTIC MODALITY
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INTRODUCTION: Adult and pediatric brain tumors are among the most fatal cancers known with limited treatment options. One of the key tumor features facilitating its growth and progression is evading the immune system. Recent data suggests that the interaction between the cell surface antigen CD47 and its binding partner SIRPa is a mechanism by which non-solid and solid tumors can evade the innate immune system. Here, we show that disrupting the interaction of this anti-phagocytic surface protein, CD47 with its interacting partner on macrophages (SIRPa) induces the macrophages to “eat and kill” brain cancer cells through modulating the innate immune system. METHODS: CD47 expression was evaluated on surgical patient and post-mortem samples from different brain tumor: Adult and pediatric Glioblastoma, Oligodendroglioma, DIPG, Medulloblastoma, Ependymoma, ATRT, PNET tissue samples were analyzed for CD47 expression. Using a novel humanized anti-CD47 monoclonal antibody we tested whether blocking CD47- SIRPa interaction induces phagocytosis. Orthotopic patient derived xenograft models were treated them with the humanized anti-CD47 mAb. Additionally, we tested the effect of huCD47-Ab antibody on normal neural cells. The ability of blocking the CD47-SIRPa axis to enhance the therapeutic response of available clinical monoclonal antibodies was also tested. RESULTS: CD47 expression was upregulated in all tumor types and was present in >90% of the cells in high-grade tumors. Blocking the CD47- SIRPa interaction increased phagocytosis by macrophages in tumor but not on normal neural cells. Systemic treatment with anti-CD47 antibody significantly reduced tumor burden and enhanced survival. NHP studies show that the huCD47 antibody can be administered safely at potentially therapeutic serum levels. CONCLUSION: Anti-CD47 therapy is a viable and effective treatment modality for human high-grade brain tumors. Currently a Phase I study is ongoing to evaluate its safety in patients with non-CNS tumors to be followed by safety in patients with CNS malignancies.