Next, we analyzed signaling molecules activated in CD11b cells pulsed with PD-L1 ± CD200AR-L, followed up with in vitro and in vivo effects of CD200AR-L on the expression of PD-1/PD-L1 and CTLA-4. Finally, we analyzed the ability of the CD200AR-L to surmount the suppressive effects of PD-L1.

Results Our studies demonstrate that the inhibitory CD200R1 and PD-1 mediate immune checkpoint signaling activities through SHIP1 protein. Moreover, CD200AR-L overpowers the suppressive effects of CD200 and PD-L1, which are both shed by tumors, by downregulating the inhibitory CD200R1 and PD-1 on both antigen-presenting cells (APC) and T-cells (figure 1). In addition, CD200AR-L downregulates PD-1 on APCs and inhibits the upregulation of PD-L1 and CTLA4.

Abstract 213 Figure 1 Mechanism of the CD200 Checkpoint Ligand

Conclusions These studies led to the discovery that this novel peptide modulates the CD200, PD-1/PD-L1 and CTLA-4 pathways, providing the basis for the translatable development of a novel CD200 peptide inhibitor for clinical use against multiple tumors, including gliomas. These studies led to the FDA approval for the first in human peptide checkpoint inhibitor to initiate a phase I single center, open-label, dose-escalation clinical trial in adult patients with recurrent glioblastoma, to be followed by a clinical trial for children with recurrent malignant brain tumors.

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THE EFFECT OF ANTI-PD-1 THERAPY ON MEDIAN OVERALL SURVIVAL AND PROGRESSION FREE SURVIVAL IN GLIOBLASTOMA MULTIFORME PATIENTS WITH CERTAIN TUMOR MARKERS

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Background Almost 1 in 6 malignant brain cancers are Glioblastoma Multiforme, relative to most other brain cancers it is the most aggressive and prevalent by the numbers.¹ Even with the best treatment options median Overall Survival(OS) remains morbid at 14.6 months and Progression Free Survival (PFS) remains 6.9 months.² Telomerase Reverse Transcriptase promoter mutations,³ Isocitrate Dehydrogenase(IDH)

mutations,⁴ and Tumor Mutation Burden(TMB)⁵ are three prominent tumor markers that are known to be associated with better PFS and OS; markers like these in the presence of new therapies maybe prove crucial to the development of novel therapies. Immunotherapy has been dubbed a 'game changer' in certain hematological and solid malignancies. Specifically, PD1 is a glycoprotein that is a strong negative regulator of the immune system, by blocking this glycoprotein Anti-PD-1 agents harness a strong response by the immune system to fight a malignancy⁶. In conjunction with these new found tumor markers, Anti-PD-1 agents maybe the solution that could dramatically improve OS and PFS in these patients.

Methods The goal of this study was to retrospectively analyze patients' charts who had received Anti-PD-1 therapy and had TERT promoter mutations, IDH mutations, different TMBs, and other markers and to compare their OS and PFS outcomes with conventional therapies and their response to immunotherapy.

Results Upon analyzing the data the presence of a TERT promoter 124C>T mutation, IDH wildtype, and lower TMB gave much better OS and PFS after treatment in patients on Anti-PD1 therapy.

Conclusions Although this was a small study, these results certainly can be used to examine larger subsets of patients with these markers receiving immunotherapy because they had definitively better outcomes as compared to status quo treatment options.

Ethics Approval The study was approved by Washington University Ethics Board, approval number 201111001.

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AO-176, A HIGHLY DIFFERENTIATED CLINICAL STAGE ANTI-CD47 ANTIBODY, PREFERENTIALLY BINDS TUMOR VERSUS NORMAL CELL CD47 WHEN COMPLEXED TO β 1 INTEGRIN

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Background Overexpression of CD47 by tumor cells exploits an immune checkpoint preventing tumor recognition and destruction by innate immune cells. Binding of tumor CD47 to SIRP α on macrophages and dendritic cells triggers a 'don't eat me' signal that inhibits phagocytosis and allows escape from innate immune surveillance. Blockade of the CD47/SIRP α axis, however, enables immune recognition and phagocytic clearance of tumor cells. We have developed a clinical stage CD47 targeting antibody AO-176 that is highly differentiated among agents in this class. AO-176 not only blocks the