PM-17. INTRACEREBRAL IFN-γ DOES NOT ENHANCE THE RESPONSE TO VACCINE IMMUNOTHERAPY FOR CANINE GLIOMA
Liz Pluhar, Michael Olin, Michelle Goulart, Brian Andersen, Matt Hunt, and John Ohlfest; University of Minnesota, Minneapolis, MN, USA

Due to the complexity of human tumor environment and host immune interactions, the majority of successful brain cancer therapies in rodent models fail to show the same efficacy when translated to human patients. Pet dogs with spontaneous glioma recapitulate important features of human disease and we have used this more representative model to assess the response to vaccine immunotherapy with and without interferon gamma (IFN-γ) gene therapy after surgery. Dogs with newly diagnosed glioma underwent surgical tumor debulking and were randomized to receive 1) autologous tumor lysate vaccines with CpG ODN as an adjuvant (n = 12) or 2) Ad-mediated interferon gamma (IFN-γ) gene therapy injected around the resection cavity followed by vaccine immunotherapy (n = 12). A grade IV IFN-γ dose-related toxicity (severe encephalitis and lymphocytic perivascular cuffing) resulted in death of one dog. No further adverse events were seen at a lower IFN-γ dose supporting the safety of the treatment. This immunotherapy activated a humoral response with specific tumor-reactive IgG antibodies detected after vaccination in all dogs. Addition of IFN-γ gene therapy did not affect the median overall survival time of 204 days versus 211 days with vaccine alone. As expected, there were significant differences (P = 0.036) in survival between dogs with low-grade (369 days) versus high-grade (204 days) tumors. During postmortem analysis, no dog with a low-grade tumor had recurrence, whereas all dogs with grade III/IV tumors died from progression. We hoped that forced IFN-γ expression would sensitize residual tumor cells to CTL recognition and recruit NK cells to kill MHC I low cells, thereby enhancing the effects of vaccine immunotherapy. Our data failed to support this theory, however the lack of difference could be due to the small number of dogs in each group (type II error) or to insufficient in situ expression of IFN-γ to elicit the desired effect.