PERSONALIZED DNA VACCINE IN COMBINATION WITH PLASMID ENCODED IL-12 FOR THE TREATMENT OF A PATIENT WITH ANAPLASTIC ASTROCYTOMA

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Background Tumor neoantigens are epitopes derived from tumor-specific mutations. Such mutations can be incorporated in personalized vaccines to prime T cell responses against tumor specific antigens. DNA vaccines delivered with electroporation have recently shown strong CD8 and CD4 T cell responses in clinical trials. In preclinical studies, DNA-encoded neoantigen vaccines have shown induction of CD8 T cells against 50% of predicted high affinity epitopes with the ability to impact tumor growth.

Methods Two resection samples from a patient with IDH+ MGMT-methylated anaplastic astrocytoma were subject to whole exome and transcriptome sequencing. Epitopes derived from 27 neoantigens and 3 shared tumor-associated antigens were prioritized and included in a personalized vaccine. The patient was treated with surgery, radiotherapy and temozolomide starting June 2018 and received the first dose of the personalized vaccine in June 2019 under a compassionate use single patient IND application with the FDA.

Results As of July 23rd, 2021, the patient has received 11 doses of the DNA personalized vaccine. No serious adverse events have been reported. Related adverse events are limited to grade 1 injection site reactions. The patient remains progression-free 37 months after surgery and 25 months after starting vaccination. Three weeks following the 3rd dose, a hyperintense image on the tumor bed was identified, which disappeared on the following MRI, 2 weeks following dose 5, being catalogued as pseudo progression. Ex vivo ELISpot have identified T cell responses to 28/30 epitopes (93.3%), including 25/27 (92.6%) neoantigens and 3/3 (100%) shared antigens. Flow cytometry analysis has determined that T cell responses are 92.3% CD8 and 69.2% CD4 (30.8% CD8 only; 61.5% both CD8 and CD4; and 7.7% CD4 only).

Conclusions This compassionate use treatment in an adjuvant setting demonstrates manufacturing feasibility, safety, tolerability, immunogenicity, and suggests potential for persistent clinical response of DNA encoded personalized vaccines. The data supports further investigation of DNA-encoded personalized vaccines into newly diagnosed high-grade gliomas.

Ethics Approval The study was approved by Washington University's IRB. The participant gave informed consent before taking part in the study.

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