Background The efficacy of T cell directed immunotherapies relies on adequate priming of T cells to tumor-specific neoantigens, which some studies have augmented with synthetic neoantigen vaccines. This is the first report of a personalized genomic vaccine (PGV-001) in multiple sequenced in the adjuvant setting.

Methods Tumor and germline RNA and DNA were sequenced, and neoantigen peptides were selected using our OpenVax custom computation pipeline that identifies and ranks mutant sequences by a combination of predicted MHC-I binding affinity and neoantigen abundance within tumor. Up to 10 peptides were synthesized per patient and were administered over the course of 27 weeks in combination with the poly-ICLC. Primary objectives were to determine 1) the safety and tolerability; 2) the feasibility of PGV-001 production and administration; and 3) the immunogenicity of PGV-001. Secondary objectives included immunophenotyping neoantigen-specific T cells in peripheral blood, and characterization of peripheral blood lymphoid, myeloid and humoral responses. We report here for the first time on the primary endpoints.

Results Vaccine was synthesized for 15 patients. A mean of 1619 somatic variants (range 521–5106) were detected. Our pipeline identified a mean of 67.1 neoantigens/patient (range 8–193) and 9.7 peptides/patient were synthesized (range 7–10). 13 patients received PGV-001 (11 patients received all 10 doses and 2 patients received at least 8 doses) while 2 had progressive disease before vaccine initiation. Transient grade 1 injection site reactions were seen in 31% of patients, and one patient experienced grade 1 fever. There were no other significant adverse events. Ex vivo ELISpot analysis of patient blood demonstrated significant induction of T cell responses following receipt of 10 vaccines that were not present after the 6th vaccine, supporting the need for a prolonged dosing schedule. Robust responses were seen in both CD4 and CD8 T cells by intracellular cytokine staining for TNF-a, IFN-a, and IL-2 following in vitro expansion in the presence of vaccine antigens. Additional studies are ongoing to define the most immunogenic neoantigens.

Conclusions A personalized neoantigen vaccine of synthetic mutant peptides and adjuvant poly-ICLC was successfully synthesized for 15 patients and administered successfully to 87% patients over the course of 27 weeks. The vaccine was well tolerated, and T cell expansion and reactivity to synthetic neoantigens confirms immunogenicity of neoantigens identified with OpenVax.

Trial Registration NCT02721043

Ethics Approval This study was approved by the IRB of The Mount Sinai Hospital in accordance with Federal law. HSM #15-00841.

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