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Neoantigens, which are derived from tumour-specific protein-coding mutations, are exempt from central tolerance, can generate robust immune responses\textsuperscript{1-3} and can function as bona fide antigens\textsuperscript{3,4} that facilitate tumour rejection\textsuperscript{3,5}. Here we demonstrate that a strategy that uses multi-epitope, personalized neoantigen vaccination, which has previously been tested in patients with high-risk melanoma\textsuperscript{4-6}, is feasible for tumours such as glioblastoma, which typically have a relatively low mutation load\textsuperscript{7,8} and an immunologically 'cold' tumour microenvironment\textsuperscript{9}. We used personalized neoantigen-targeting vaccines to immunize patients newly diagnosed with glioblastoma following surgical resection and conventional radiotherapy in a phase I/IIb study. Patients who did not receive dexamethasone-a highly potent corticosteroid that is frequently prescribed to treat cerebral oedema in patients with glioblastoma-generated circulating polyfunctional neoantigen-specific CD4\textsuperscript{+} and CD8\textsuperscript{+} T cell responses that were enriched in a memory phenotype and showed an increase in the number of tumour-infiltrating T cells. Using single-cell T cell receptor analysis, we provide evidence that neoantigen-specific T cells from the peripheral blood can migrate into an intracranial glioblastoma tumour. Neoantigen-targeting vaccines thus have the potential to favourably alter the immune milieu of glioblastoma.

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