Neoantigen vaccine generates intratumoral T cell responses in phase Ib glioblastoma trial -
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Neoantigens, which are derived from tumour-specific protein-coding mutations, are exempt from central tolerance, can
generate robust immune responses and can function as bona fide antigens that facilitate tumour rejection. Here we
demonstrate that a strategy that uses multi-epitope, personalized neoantigen vaccination, which has previously been
tested in patients with high-risk melanoma, is feasible for tumours such as glioblastoma, which typically have a
relatively low mutation load and an immunologically ‘cold’ tumour microenvironment. 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+ and CD8+ 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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