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A peptide vaccine targeting the CMV antigen pp65 in children and young adults with recurrent high-grade glioma and medulloblastoma: a phase 1 trial

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Abstract

The human cytomegalovirus (CMV) antigen pp65 is expressed in high-grade glioma (HGG) and medulloblastoma but not in the adjacent brain. This single-arm phase 1 trial (NCT03299309) assessed the safety and immunogenicity of a peptide vaccine (PEP-CMV) targeting pp65 in individuals (3-35 years old) with recurrent HGG or medulloblastoma. Thirty-six individuals with HGG received PEP-CMV. The mean age was 22.75 ± 9.34 years. The primary outcome, percentage of unacceptable toxicity, was met. The maximum-grade adverse events (AE) related to PEP-CMV were 17 grade 1 AEs, 15 grade 2 AEs, 1 grade 3 AE (pyramidal tract syndrome) and 1 grade 4 AE (cerebral edema). As a secondary outcome, in 21 individuals with evaluable data, T cell reactivity, measured as change in baseline interferon-γ pp65 enzyme-linked immunospot assay reactivity, had an estimated increase of 46 spots (95% confidence interval (95% CI): 8, 194) after treatment with PEP-CMV. As exploratory endpoints, the median progression-free survival was 2.5 months (95% CI: 2.2, 3.2), and median overall survival was 6.5 months (95% CI: 4.6, 8.4). PEP-CMV is well tolerated and elicits an antigen-specific immune response in individuals with multiply recurrent HGG. Only two individuals with medulloblastoma were enrolled, showing one grade 3 encephalopathy possibly related to PEP-CMV, while neither had postvaccine immune assessments due to progression-free survival and overall survival less than 2 months.