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A combinatory vaccine with IMA950 plus varlilumab promotes effector memory T-cell differentiation in the peripheral blood of patients with low-grade gliomas

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Abstract

Background: Central nervous system (CNS) WHO grade 2 low-grade glioma (LGG) patients are at high risk for recurrence and with unfavorable long-term prognosis due to the treatment resistance and malignant transformation to high-grade glioma. Considering the relatively intact systemic immunity and slow-growing nature, immunotherapy may offer an effective treatment option for LGG patients.

Methods: We conducted a prospective, randomized pilot study to evaluate the safety and immunological response of the multi-peptide IMA950 vaccine with agonistic anti-CD27 antibody, varlilumab, in CNS WHO grade 2 LGG patients. Patients were randomized to receive combination therapy with IMA950+poly-ICLC and varlilumab (Arm 1) or IMA950+poly-ICLC (Arm 2) before surgery, followed by adjuvant vaccines.

Results: A total of 14 eligible patients were enrolled in the study. Four patients received pre-surgery vaccines but were excluded from post-surgery vaccines due to the high-grade diagnosis of the resected tumor. No regimen-limiting toxicity was observed. All patients demonstrated a significant increase of anti-IMA950 CD8 + T-cell response post-vaccine in the peripheral blood, but no IMA950-reactive CD8 + T-cells were detected in the resected tumor. Mass cytometry analyses revealed that adding varlilumab promoted T helper type 1 effector memory CD4 + and effector memory CD8 + T-cell differentiation in the PBMC but not in the tumor microenvironment.

Conclusion: The combinational immunotherapy, including varlilumab, was well-tolerated and induced vaccine-reactive T-cell expansion in the peripheral blood but without a detectable response in the tumor. Further developments of strategies to overcome the blood-tumor barrier are warranted to improve the efficacy of immunotherapy for LGG patients.

Keywords: IMA950; immunotherapy; low-grade glioma; poly-ICLC; varlilumab.