STRONG IMMUNE RESPONSE TO THERAPEUTIC VACCINATION WITH EO2401 MICROBIOME DERIVED THERAPEUTIC VACCINE + NIVOLUMAB: INTERIM REPORT OF THE EOGBM1–18/ROSALIE STUDY

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Background EO2401 is a therapeutic vaccine designed to activate memory commensal specific T-cells that are cross-reacting against validated tumor associated antigens (TAAs). EO2401 includes synthetically produced HLA-A2 peptides with molecular mimicry to TAAs (IL13Ra2, BIRC5 and FOXM1) upregulated in glioblastoma, and the CD4 helper peptide UCP2.

Methods Patients with glioblastoma at first progression after radiotherapy/temozolomide received EO2401 with nivolumab (EN), or EN with bevacizumab within trial EOGBM1-18 (NCT04116658). Blood collection was performed at baseline and then every two or four weeks. Immune responses were investigated either directly on cryopreserved PBMCs without stimulation (ex vivo), or after 12 days in vitro stimulation (IVS) using tetramer staining, IFNγ ELISpot and intracellular cytokine staining. The study was approved by all participating institution’s Ethics Boards.

Results Immune monitoring in EO2401 vaccinated patients demonstrates the ability of bacterial peptides to induce a strong CD8+ T cell response with cross-reactivity against human selected TAAs. Immune response against the 3 microbiome-derived peptides is demonstrated for 28 of 29 investigated patients using ELISpot after IVS. Post vaccination frequency of CD8+ T cells against bacterial peptide after IVS is extremely high, with a median of 5.5% of specific CD8+ T cells for EO2316 (max 18%), 16% for EO2317 (max 46%) and 14% (max 40%) for EO2318. Cross-reactivity against the pool of human peptides is demonstrated in 27/28 patients using ELISpot after IVS and validated using tetramer staining against BIRC5 and FOXM1. Polyfunctionality of CD8+ T cells effectors is supported by frequent expression of CD107a as well as IFN-γ and TNF-a production after stimulation. Ex vivo, CD8+ T cells against at least one of the EO2401 peptides are detected in 26/28 evaluable patients with some patients exhibiting up to 5% of circulating specific CD8+ T cells. Memory specific CD8+ T cells response are found as early as two weeks after the first vaccination and maintenance of a strong and stable immune response could be detected for more than 10 months. CD4+ T cell response against the UCP2 helper peptide is demonstrated using IFN-γ ELISpot after IVS.

Conclusions EO2401 vaccine demonstrates ability to generate fast and durable immune responses in patients treated with EO2401/nivolumab +/- bevacizumab. Activation of specific T cells cross-reacting against commensal antigens and TAAs is thereby validated as an efficient approach to activate strong immune responses in a difficult to treat tumor with low neo-antigen expression and poor T cell priming.

Trial Registration NCT04116658

Ethics Approval This study has obtained an ethics approval (Dana Farber Cancer Institute IRB: iRIS number 438532) and all participants gave informed consent before taking part.