Background: EO2401 was designed to activate memory T cells cross-reacting with tumor associated antigens. EO2401 includes synthetically produced HLA-A2 peptides with molecular mimicry to antigens (IL13Rα2, BIRC5 and FOXM1) upregulated in glioblastoma, and the CD4 helper peptide UCP2.

Methods: Patients with glioblastoma at first progression after radiotherapy/temozolomide received EO2401 (300 μg/peptide, q2w x4 then q4w) with nivolumab (3 mg/kg q2w; EN regimen), or EN with bevacizumab (10 mg/kg q2w; ENB regimen). In study part 2, low-dose bevacizumab (LDB) (5 mg/kg q2w up to 6 doses) could be used as symptom directed treatment of edema. The study, NCT04116658, was approved by all participating institution’s Ethics Boards.

Results: Part 1 included 40 patients (EN = 29, ENB = 11). Part 2 enrolled 36 patients treated with EN, and the possibility of symptom directed LDB. In study part 3, 15 further patients are to be treated with ENB (enrollment ongoing).

EN and ENB were well tolerated with EO2401 associated toxicities limited to local administration site reactions (45% of patients; events 70% Grade 1, 26% Grade 2, and 4% Grade 3). The frequency and severity of nivolumab-/bevacizumab-toxicities was consistent with historical single-agent data. Immune monitoring demonstrated positive responses against the 3 microbiome-derived peptides for 28 of 29 patients investigated ex vivo or after in vitro stimulation (IVS). For some patients, positive response was already detected two weeks after the first vaccination and was maintained for more than 10 months. Cross-reactivity against the pool of 3 human target peptides was demonstrated in 27 of 28 patients using IFN-γ ELISpot assay.

For part 1, median progression-free survival (mPFS), and median survival for EN (n=29, median follow-up 14.0 months) were 1.8 and 10.6 months. Patients on ENB (n=11, median follow-up 9.6 months) had mPFS of 5.5 months and 9 patients were alive (7-12.4 months). Objective Response Rate (ORR)/Disease Control Rate (DCR) (ORR + stable disease) for EN and ENB were 10%/34% and 55%/82%.

Median treatment duration for EN in part 1 was 8.9 weeks (2 of 29 on treatment), while it was 12.0 weeks (21 of 36 on treatment) in part 2. Overall, in part 2, 13 patients (36%) received LDB.

Conclusions: EO2401 was well tolerated and generated fast and durable immune responses in most patients. Addition of standard bevacizumab to EN improved PFS and ORR/DCR. Symptom directed LDB supported longer treatment durations.

Updated safety, immunogenicity, and efficacy data from all parts of the trial will be presented.

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.