

Clinical Trial In Progress

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EO2401, A NEW PEPTIDE IMMUNOTHERAPY AGAINST CANCER, IN COMBINATION WITH NIVOLUMAB, INDUCES A STRONG AND DURABLE IMMUNE RESPONSE IN PATIENTS FROM THE EOADR1–19/SPENCER STUDY

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Background EOADR1–19/SPENCER study is a phase 1/2 trial of EO2401, evaluating the combination of EO2401 with nivolumab, for the treatment of patients with locally advanced or metastatic adrenocortical carcinoma (ACC) or malignant pheochromocytoma/paraganglioma (MPP). EO2401 is a novel immunotherapy designed to activate memory T cells specific to gut microbiota derived peptides crossreacting with tumor-associated antigens (TAAs). EO2401 comprises three HLA-A2 restricted peptides derived from commensal proteins (EO2316, EO2317 and EO2318), mimicking three TAAs overexpressed in adrenal tumors: IL13RA2, BIRC5 and FOXM1. The study (NCT04187404) was approved by all participating institution's Ethics Boards.

Methods Blood samples were collected at baseline, every two weeks during the first 3 months, then every month until disease progression. Immune response in cryopreserved PBMCs was investigated using tetramer staining and IFN γ ELISpot ex vivo and after in vitro stimulation (IVS). The functionality of specific CD8⁺T cells was also studied through cytotoxic T-cell based killing assays using T2 cells and intracellular cytokine staining (ICS) after IVS.

Results The efficacy of EO2401 in generating immune responses against TAAs was studied ex vivo or after IVS. Commensal-specific T cells were detected through tetramer staining against at least one peptide in 92% of tested patients (35/38) while TAA specific T cells were observed in 88% of tested patients (32/36). Positivity could be detected as early as two weeks after the treatment initiation (with 1 injection) and maintained for at least 20 months (longer follow up). The most immunogenic peptides were EO2317 and EO2318 with 80% and 72% of responding patients respectively. Lower immunogenicity was observed for EO2316. Moreover, when investigated using IFN γ ELISpot, 87% and 80% of patients showed functional T cells against the pool of commensal-derived peptides or of TAAs. Notably, generated antigen specific CD8⁺ T cells observed ex vivo displayed a memory phenotype (TEM and TEMRA). Finally, cytotoxic killing assays using T2 cells loaded with commensal-derived peptides, showed that to date, 3 out of 4 patients tested presented a specific killing of T2 cells correlated with a strong capacity of cytokine production (ICS) after IVS.

Conclusions EO2401, in combination with nivolumab induces fast, strong and long-lasting immune response, with detection of bacterial peptide- and TAA- specific functional CD8⁺ T cells in almost all patients. These results highlight the potential of this innovative approach to overcome the limitations of current cancer vaccine strategies.

Ethics Approval The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of CPP Ouest II Angers – France (ref 19.10.18.72055 – 2020/25); the Ethics Committee of Hospital Universitari Vall d'Hebron - Spain; the Ethics Committee of Universität Würzburg - Germany (ref 264/19_m); the Ethics Committee of Di Brescia – Italy; the Ethics Committee from the Center for Regional Udvikling – Denmark (ref: H-20003010); the CCMO – Netherlands (ref: CCMO20.021/JvG/rm/71766); the Överklagandenämnden för etikprövning – Sweden (Dnr 34–2020/3.1) and the Institutional Review Board from the Office of Human subject Protection of MD Anderson Center (IRB ID: 2020–0054).

Consent All subjects gave their informed consent for inclusion before participating in the study

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