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A phase II study of cancer vaccination using three peptides combination with gemcitabine as a first-line therapy for advanced pancreatic cancer (VENUS-PC study)

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Background: The novel HLA-A*2402-binding peptides derived from KIF20A (RAB6KIFL) belong to the kinesin superfamily of motor proteins, which play critical roles in the trafficking of molecules and organelles during the growth of pancreatic cancer (PC). A phase I cancer vaccination trial using KIF20A determined its safety and immunogenicity in advanced PC patients (J Immunother 2014;37:36−42). We further conducted a phase II trial using not only KIF20A but also an antiangiogenic cancer vaccine targeting VEGFR1 (vascular endothelial growth factor receptor 1) and VEGFR2. These two peptides had revealed the safety and immunogenicity in advanced colorectal cancer (J Transl Med. 2014; 12:63). We try to evaluate the benefit of the cancer vaccination in combination with gemcitabine (GEM) as a first-line therapy in advanced PC patients.
Methods: Chemotherapy naïve PC patients were enrolled to evaluate primarily the one year survival rate, and secondarily the induction of specific immune responses. Each of the three peptides was mixed with 1ml of Incomplete Freund's adjuvant and subcutaneously administered weekly. GEM was administered at a dose of 1000 mg/m^2 on days 1, 8, and 15 in a 28-day cycle. All enrolled patients received the therapy without knowing the HLA-A status, and the HLA genotypes were revealed at analysis point, and then the endpoints were evaluated between the HLA-A*2402 matched and HLA-A*2402 unmatched group.
Results: Between June 2012 and May 2013, a total of 68 patients were enrolled in this study. No severe adverse effects of grade 3 or higher related to these three peptides were observed. The one year survival rate was not significantly different between the HLA-A*2402-matched and unmatched groups ($p = 0.456$). Peptides-specific IFN-g response was not observed in the HLA-A*2402-unmatched group. In the HLA-A*2402-matched group, patients observed with specific IFN-g responses for KIF20A or VEGFR2 had the better prognosis compared to those without them. In the subgroup analysis of the HLA-A*2402-matched group, the patients who revealed strong injection site reaction (i.e., induration, erosion) had the better survival ($p = 0.017$) compared to those without injection reaction.
Conclusions: Specific IFN-γ response (secondary endpoint) for KIF20A or VEGFR2 was observed in some patients of the HLA-A*2402-matched group, and this response seems to be associated with the better prognosis, although significant difference in the one year survival was not observed in each groups. Moreover, in the HLA-A*2402 matched group, the patients who revealed strong injection site reaction had the better survival. This phase II cancer vaccine therapy demonstrated that our therapeutic peptides cocktail was likely to be effective in a subset of patients. Predictive biomarkers will be needed for selecting patients to have a better treatment outcome with the vaccination.
No conflict of interest.

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MVX-ONCO-1: First in man, Phase I clinical trial combining encapsulation cell technology and irradiated autologous tumor cells for personalized cell-based immunotherapy. Safety, feasibility and clinical outcome results

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Introduction: Preclinical data shows that sustained, local release of muGM-CSF, at the site of immunization by irradiated, genetically engineered tumor cells leads to specific, long lasting anti-tumor immunity in all tumor types. Providing stable, prolonged, reproducible level of adjuvant in the clinical setting is very challenging. Encapsulation Cell Technology (ECT) is a novel anti-tumor immunotherapy platform allowing sustained, controlled and reliable delivery of potent stimulatory proteins by immunoprotected allogeneic cells. We developed MVX-ONCO, a clinical grade ECT product for the sc delivery of huGM-CSF at the vaccination site, a key factor for successful immunization. MVX-ONCO-1 is the very first clinical trial assessing this novel, patient specific, cell-based therapy, combining the sc implantation of irradiated autologous tumor cells and 2 macrocapsules containing allogeneic cells genetically engineered to produce huGM-CSF.
Methods: 15 pts with progressing, solid tumors refractory or not amenable to standard chemotherapy are enrolled to evaluate safety, feasibility and clinical outcome. Immunizations are performed in healthy skin, distant from tumor deposits. Pts are treated with 6 sc immunizations (week 1−2-3−4-6−8) combining $4x10^6$ irradiated autologous tumor cells and 2 macrocapsules containing each $8x10^5$ MVX-1 cells, producing >20ng/24h of huGM-CSF. Macrocapsules are removed after 7 days and analyzed for huGM-CSF production. Both macrocapsules loaded with MVX-1 cells and irradiated autologous tumor cells, harvested from ascites, pleural fluid or surgical samples are processed and stored frozen.
Results: As of April 28 2015, 8 pts are available for safety and feasibility analysis. No safety issue is observed regarding the experimental therapeutic product. Main toxicity is minor local discomfort during the macrocaspules sc implantation. None of the reported SAEs are related to the immunizations. Production of both irradiated autologous tumor cells and MVX-1-containing macrocapsules are successful in all pts. None of the prepared therapeutic vaccine had to be discarded due to quality concern. 100% of explanted macrocapsules produced high ex-vivo huGM-CSF production. 4 out of 6 pts evaluable for clinical outcome, presented some clinical benefit (stable disease >2 months, decrease serum tumor marker, prolonged survival).
Conclusion: This first in man trial shows the very good safety profile and also the feasibility of this novel patient specific cell-based immunotherapy. Secondary endpoints show clinical benefit for a significant portion of patients with advanced, progressing, refractory solid malignancies. Phase 2 trials with MVX-ONCO-1 are planned in several tumor types as well as combination therapies with immune check-point inhibitors. Data on all 15 patients will be presented at the meeting.
Conflict of interest: *Ownership: Founder and stock owner of MaxiVAX SA, a small start-up company based in Geneva, Switzerland and sponsor of the presented trial.*

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Skin infiltrating lymphocytes as an early biomarker to predict clinical outcome in stage III melanoma patients receiving adjuvant dendritic cell vaccination

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Background: Dendritic cells (DC) are the most efficient antigen-presenting cells of the immune system. DC can be generated ex vivo, activated, loaded with tumor antigens, and then injected into patients. With upcoming immunotherapeutic options, including DC vaccination, it is important to have relevant biomarkers to predict treatment outcome. Aim of this study