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Presentation Title: Immune responses in cancer patients after vaccination with the therapeutic telomerase-specific vaccine Vx-001.

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Background: Vx-001 (Vaxon Biotech, Genopole, Evry, France), an HLA-A*0201 restricted therapeutic telomerase-specific tumour vaccine is composed of the 9mer cryptic $TERT_{572}$ peptide and its optimized variant $TERT_{572Y}$ which exhibits a high HLA-A*0201 affinity and strong immunogenicity. We have previously shown that Vx-001 is non-toxic, highly immunogenic and Vx-001 specific immune response was correlated with prolonged survival in vaccinated NSCLC patients. In the present study we report on the further analysis of the Vx-001 specific-T cell immune responses in HLA-A*0201 patients with advanced solid tumors vaccinated with the Vx-001 vaccine. **Methods:** 97 patients with various types of cancer were vaccinated 2 sc. Administration of the optimized $TERT_{572Y}$ peptide followed by 4 vaccinations with the native $TERT_{572}$ peptide at 3 week intervals. Patients who completed the six-vaccination schedule and exhibited disease stabilisation received booster vaccinations with the native peptide every 3 months. Peripheral blood mononuclear cells, from patients were collected before vaccination, after the 2^{nd} and 6^{th} vaccination and before each boost and screened for reactivity to the $TERT_{572Y}$ and $TERT_{572}$ peptides by measuring IFN-g production using ELISpot assay and intracellular staining. Also, peptide-specific $CD8^+$ T cells were identified by $TERT_{572Y}$-pentamer and IL-10 intracellular staining using flow cytometry. **Results:** Seventy-eight (80%), seventy-nine (81%) and forty-seven (48%) patients had evaluable samples for immune response before vaccination and after the 2^{nd} and 6^{th} vaccination, respectively. $CD8^+$ T cell responses were detected in 24 (30%) patients before vaccination, in 46 patients (58%) patients after the 2^{nd} vaccination and 37 (79%) patients after the completion of 6 vaccinations, as revealed by IFN-g ELISpot assay. Intracellular staining for IFN-g and $TERT_{572Y}$-pentamer staining confirmed these responses. Immune responses detected after the 6^{th} vaccination did depend neither on the disease stage nor on the disease status before vaccination. Surprisingly, patients who did not show $TERT_{572}$-specific IFN-g immune response before vaccination responded more frequently after the 2^{nd} vaccination than patients with prevaccination detectable $TERT_{572}$-specific IFN-g immune response. Moreover, the presence of IL-10 producing T cells was inversely correlated with the development of an early vaccine-induced IFN-g immune response. Finally, prolonged vaccination maintained the number of peptide-specific $CD8^+$ T cells in the majority of patients. **Conclusion:** The Vx-001 vaccine can induce $TERT_{572}$-specific $CD8^+$ T cell immune responses in the majority of vaccinated cancer patients. This vaccine should be investigated further as it may represent a promising candidate for cancer immunotherapy.

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