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Transitory response to vaccination with PSCA-/PSA-peptide loaded, autologous dendritic cells in patients with metastatic, hormone-refractory prostate cancer

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Clinical trials employing vaccination with prostate-specific membrane antigen (PSMA) loaded dendritic cells (DC) in patients (pts) with advanced prostate cancer yielded response rates of >30%. We decided for HLA-A2 restricted peptides derived from prostate stem cell antigen (PSCA) and prostate specific antigen (PSA 1–3) because both antigens are overexpressed in >85% of prostate cancer and were demonstrated to induce antigen specific T-cell responses in vitro. Cell penetrating peptide (CPP) is a peptide derived from the HIV-tat protein that prolongs antigen presentation in vitro leading to enhanced antitumor immunity in vivo. Therefore, half of the pts were assigned to receive CPP-PSCA loaded DCs. The purpose of this study is to assess feasibility, patient safety, PSCA-/PSA-specific T-cell responses and tumor regression *in vivo*. Pts were vaccinated s.c. in 14d intervals. Response was assessed two weeks after the 4th vaccination. Delayed-type hypersensitivity (DTH) was tested d4+d46. Immune competence was monitored by HBV vaccination d1+d43. So far, 9/12 planned pts completed vaccination. No toxicities were observed. 5/9 pts achieved SD (3 with <50% decrease, 2 with <50% increase in PSA), and 3 of these but no non-responders developed a positive DTH after the 4th vaccination. The addition of CPP did not correlate with outcome. Responding pts received at mean two further vaccinations 4 weeks apart. At a median follow-up of 8.6 months 70% of pts are alive compared to a reported OS of 59% and 28% at a follow-up of 6 and 11 months, respectively for pts with metastatic, hormone-refractory disease [1-3]. No peptide specific T-cells were detected in two pts evaluated so far, however, the correlation of clinical and DTH responses suggests a tumor specific immunity. Our data indicate that vaccination with PSA/PSCA-peptide-loaded, autologous DCs is safe and well tolerated. Vaccination of more patients, long-term follow-up and completion of immune monitoring are needed to evaluate anti tumor effects.

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