Cancer vaccines with hTERT and Survivin mRNA transfected fast DCs - a simplified and effective cancer vaccine

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Prostate cancer (PC) is the most common cancer among men. Since 2005 more than 4000 new cases each year are diagnosed with PC in Norway and the incidence is increasing. In many cases prostate cancer is an indolent disease and patients often will die with the disease and not off it. If the patients are diagnosed with high Gleason Score they will develop relapse following primary therapy and when this occur there is no curative treatment available. We have previously reported that about 50% of hormone resistance patients mount specific immune responses following vaccination with Dendritic Cells (DCs) transfected with mRNA from autologous tumour. Immune responses were also related to overall survival. Initially DCs were produced over 7 days. Recently, we have reduced the production time down to 3 days (Fast DCs) and here we report about our clinical experiences with this new type of DCs. Five metastatic prostate cancer patients have been included in the study. Prior to the DC vaccination, 3 patients had bone metastasis while 2 were diagnosed with lymph node metastasis. The fast dendritic cells (DC) is produced by differentiation of autologous monocytes to mature DCs by adding GM-CSF (2500IU/mL) and IL-4 (1000IU/mL) for 48 hours, and 24 hours of maturation with GM-CSF (2500IU/mL), IL-4 (1000IU/mL), TNF-α (10ng/mL), IL-1β (10ng/mL) and PgE2 (1ug/mL) in CellGro DC medium. Mature Fast DCs were then transfected with hTERT- and Survivin-mRNA by electroporation. After over night incubation in medium without any cytokines added the vaccines were frozen and stored until use. Quality control of the DCs was performed. All mRNA transfected DC (mDCt) showed a mature phenotype with down-regulation of CD14 and up-regulation of CD80, CD83, CD86, CCR7, CD274, CD40 and HLA-DR compared to monocytes. All mDCt showed migration capacity towards CCL19. mDCt had no IL-12p70 secretion and except for one patient with high IL-10 secretion all showed low levels of IL-10. When immune responses were tested by T-cell proliferation, no CD4 T-cell responses could be detected. Two of the patient was HLA-A2 positive and dextramers was used to detect antigen specific CD8 positive T-cells in blood at several time points during the vaccination. Progression free survival (PFS) assessed by PSA measurement and MRI of the 5 patients were 7, 21, 24, 35 and 36 months. The patient vaccinated with DCs secreting high IL-10 has the shortest PFS. Two of the patients have been continuously vaccinated and one patient has been revaccinated following a treatment interval with chemotherapy and local radiotherapy of bone metastasis. Altogether, our fast DCs show objective clinical benefit in some of the patients. Only 2 patients were HLA-A2 positive and in both T-cell responses could be measured by dextramers during the vaccination. The reasons for the lack of CD4T-cell responses in our patients are not fully understood and are under investigation.