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Vaccination with WT1 induces high frequency memory and effector T cells in peripheral blood and bone marrow associated with complete remission of recurrent AML

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The transcription factor Wilms tumor protein 1 (WT1) is an interesting antigen for use in vaccination and T cell therapy in myeloid leukemias. WT1 is strongly expressed in the majority of myeloid leukemic blasts and is a key molecule for blast proliferation. A phase I/II study has been initiated in our institution in patients with acute myeloid leukemia to analyze the immunogenicity and toxicity of WT1 126–134 peptide vaccination ín combination with the adjuvants GM-CSF and keyhole limpet hemocyanin. We report here on the first 4 patients who have completed vaccination and have received a total of 15, 12, 5, and 5 vaccination cycles, respectively. While, following chemotherapy, patients 1 and 2 both had 5–10% blasts in bone marrow when vaccination was initiated, patient 3 and 4 had 90% and 70% blasts, respectively. Induction of high frequency T cell responses was detected in 3 of 4 patients with up to 0.92%, 0.43%, and 0.42% in peripheral blood and up to 0.8% in bone marrow by tetramer analysis. Detailed phenotypical analysis in patient 1 showed that WT1-specific peripheral blood T cells were almost exclusively CD45RA+CCR7-granzymeB+, and directly produced IFNγ in response to WT1 peptide, resembling cytotoxic effector T cells, while in the bone marrow both WT1-specific effector and CD45RA-CCR7- effector memory T cells were found. Patient 3 and 4 had progressive disease after 5 vaccinations. Patient 1 who had progressed during the first 4 weeks of vaccination with an increase of blasts to 30% in bone marrow was induced into complete remission after 6 vaccinations, which lasted for 12 months. Patient 2 is in continuous remission for currently 20 months. WT1 transcripts in bone marrow and peripheral blood were quantitated by PCR to monitor residual disease. In accordance with the clinical course in patients 1 and 2 we observed an approximately 100-fold, and 50-fold reduction, respectively, of WT1 transcripts following vaccination. No side effects as those typically seen with GM-CSF were noted. Taken together, these findings underline the efficacy of the vaccine, inducing high frequency WT1-specific effector and memory T cells in peripheral blood and bone marrow associated with complete remission of leukemia in the absence of hematological or renal toxicity.