Combination of chemotherapy with cancer vaccines is currently regarded as a potentially valuable therapeutic approach for the treatment of some metastatic tumors, but optimal modalities remain unknown. We designed a phase I/II pilot study for evaluating the effects of dacarbazine (DTIC) on the immune response in HLA-A2 restricted melanoma disease-free melanoma patients who received anticancer vaccination 1 day following chemotherapy (800 mg/mq i.v.). The vaccine, consisting of a combination of HLA-A2 restricted melanoma antigen A (Melan-A/MART-1) and gp100 analog peptides (250 µg each, i.d.), was administered in combination or not with DTIC to 2 patient groups. The combined treatment is nontoxic. The comparative immune monitoring demonstrates that patients receiving DTIC 1 day before the vaccination have a significantly improved long-lasting memory CD8+ T cell response. Of relevance, these CD8+ T cells recognize and lyse HLA-A2/Melan-A1 tumor cell lines. Global transcriptional analysis of peripheral blood mononuclear cells (PBMC) revealed a DTIC-induced activation of genes involved in cytokine production, leukocyte activation, immune response and cell motility that can favorably condition tumor antigen-specific CD8+ T cell responses. This study represents a proof in humans of a chemotherapy-induced enhancement of CD8+ memory T cell response to cancer vaccines, which opens new opportunities to design novel effective combined therapies improving cancer vaccination effectiveness.

Key words: chemoimmunotherapy.