Dendritic cell-based vaccines for metastatic cancer

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Dendritic cells (DC) are the most effective initiators of immune responses and their generation *in vitro* has renewed the interest in immunotherapy for cancer. Indeed, many promising clinical results have been achieved and much is still expected. Here we describe the results of a protocol using autologous tumor and allogeneic dendritic hybrid cell vaccination every 6 weeks, with at least two doses, for metastatic melanoma and renal-cell carcinoma patients. Seventy patients were enrolled between March 2001 and December 2004. Half of the patients received the vaccine alone (until March 2003), and the other half received a single dose of cyclophosphamide before each vaccine dose and, after the second vaccine dose, a 5-day course of low dose IL-2 starting on the vaccination day. In each group 30 patients received the intended treatment of, at least, two vaccine doses. Response rates and patterns were not significantly different between the two groups. Though all patients included presented large tumor burdens and progressive diseases, 82% of them experienced clinical benefit from the vaccination, with disease stabilization up to more than 22 months. The median time to progression was 5.7 months and no significant untoward effects were noted. Furthermore, immune function, as evaluated by cutaneous delayed-type hypersensitivity reactions to recall antigens and by peripheral blood proliferative responses to tumor-specific and non-specific stimuli, presented a clear tendency to recover in vaccinated patients. Also, dendritic cell differentiation and function showed a significant recovery in the vaccinated patients. These data indicate that dendritic-tumor hybrid cell vaccination affects the natural history of advanced cancer and provide support for its study in less advanced patients, who should, more likely, benefit to a greater extent from this approach.