Dendritic Cell-Based Immunotherapy Combined with Sunitinib for Metastatic Renal Cell Carcinoma

Introduction and Objective: While molecular targeted drugs are mainstay for the treatment of metastatic renal cell carcinoma (mRCC), immunotherapy is still a promising treatment option. Based on experimental findings which show synergistic effect of sunitinib on immune-based cancer therapy, we conducted a phase I clinical trial of DC-based immunotherapy combined with sunitinib for patients with mRCC.
Materials and Methods: Patients with mRCC prior to a nephrectomy were enrolled. Vaccines were generated from autologous monocyte-derived DCs which were loaded with autologous tumor lysate by electroporation. Vaccines were given subcutaneously weekly for six times. Sunitinib was administered by a standard regimen. The primary endpoint was safety, and the secondary endpoint was immunological response and clinical outcome. The protocol was approved by institutional review board. Immunological response was evaluated by delayed type hypersensitivity (DTH), and antigen-specific T cell response was assessed by IFN-γ secretion assay. Serum cytokines were evaluated flowcytometry-based assay. Myeloid derived suppressor cells (MDSC) and regulatory T cells (Treg) in the peripheral blood were evaluated by flowcytometry.
Results: Seven patients were enrolled in the study. One patient had unclassified RCC, while the other six had clear cell RCC. Two patients were categorized into MSKCC poor risk and the other five into intermediate risk. Vaccination was well-tolerated and no vaccination-related toxicity or autoimmunity was noted. With a median follow-up of 7.7 months (range 4.8-15.8), three patients died of cancer and one died of sunitinib-related cerebral hemorrhage. Best response to the therapy was CR in 1, PR in 1, SD in 4 and PD in 1 patient. Only two patients showed positive DTH reaction. By IFN-γ secretion assay, tumor-specific CD4 or CD8 T cell responses were noted in 4 patients. Peripheral MDSCs were decreased in 5 patients whereas Treg did not change. Three cases with high serum interleukin-8 concentration seemed to have decreased CD4/8 response.
Conclusion: DC-based vaccination was well-tolerated. DC-based immunotherapy combined with sunitinib showed moderate clinical effects. Regarding the immunological response, sunitinib may play a role in decreasing number of MDSCs. Serum interleukin-8 may be a negative predictor for tumor-specific immunological response.