Phase I/IIa clinical study of autologous dendritic cell therapy in patients with relapsed or refractory multiple myeloma

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Cellular immunotherapy using dendritic cells is emerging as a useful immunotherapeutic modality to treat multiple myeloma (MM). We have developed potent immunotherapeutic agent (VAX-DC/MM) generated by dendritic cells loaded with the ultraviolet B-irradiated autologous myeloma cells. In this study, we evaluated the safety and efficacy of VAX-DC/MM in patients with relapsed or refractory MM. This trial enrolled relapsed or refractory MM patients who had received thalidomide- and bortezomib-containing regimen. Patients received the intradermal VAX-DC/MM injection every week for four weeks. Before the first injection of VAX-DC/MM, low-dose cyclophosphamide (375 mg/m^2, i. v) was administered to stimulate immune response at D-3. In a phase I trial, each three patients were treated with 5 x 10^6, and 10 x 10^6 cell, respectively. After higher dose was established as the tolerable dose, an additional 6 patients were enrolled at 10 x 10^6 cell doses. Median time to VAX-DC/MM therapy from diagnosis was 56.6 months (28.5-130.5). Patients had received a median of five prior treatments, and 75% had received autologous stem cell transplantation. VAX-DC/MM therapy was well tolerated, and most frequent adverse event was grade 1-2 myalgia (33.3%). In 8 of 9 patients who received 10 x 10^6 cell, immunologic response (88.9%) was observed by interferon-gamma ELISPOT assay or mixed lymphocyte reaction assay for T-cell proliferation. Clinical benefit rate was 66.7% including 1 minor response (11.1%) and 5 stable disease (55.6%), and 3 patients (33.3%) showed a progression disease. The median progression free survival was 3.1 months (95% CI, 2.8-3.5 months), and all patients are alive. In conclusion, VAX-DC/MM therapy was well-tolerated, and has activity in heavily pretreated MM. Further studies are needed to increase the efficacy of VAX-DC/MM in patients with MM.

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