657 A COMBINATION TREATMENT OF BONE MARROW-DERIVED CD141^{+}DENDRITIC CELLS AND PD1/PD-L1 INHIBITORS FOR EFFECTIVE IMMUNOTHERAPY FOR SOLID TUMORS

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Background Dendritic cells (DCs) vaccines are highly anticipated new anti-cancer therapies that can provide alternatives to existing immunotherapy methods. In immunotherapy using DCs, most preceding studies and clinical trials have been conducted with monocyte-derived DCs (MoDCs) due to their safety and accessibility, but significant effects have not been approved. Among various DC types, CD141^{+}DC (cDC1) is expected to be effective due to its antigen-presenting ability and induction to directly kill cancer by priming and activating the CD8^{+}T cell and CD4^{+}T helper cell. However, cDC1 only exists in very small amounts in the body. To overcome these limitations, we developed DC vaccine using bone marrow that shows high CD141^{+} expression. In addition, by using, WT1 protein as an antigen, which is expressed in 80% of solid cancers, it can be applied to various solid cancers.

Methods Cell culture: DCs were derived from bone marrow, and to target various solid cancers, WT1 protein expressed in most solid cancers was used as an antigen, and maturation factor was used to induce maturation of immature DCs. Naive T cells were isolated from Human peripheral blood mononuclear cells. IL-2 was used for proliferation, lasting about 10–14 days.

Phenotypic analysis flow cytometry was used to analyze the DC and T cell phenotype.

Mesuring cytokine secretion The concentration of cytokines was measured using commercial Quantikine ELISA kits to detect IFN-γ and IL-12p70, which are secreted in T cell and T cell + DC co-culture supernatant.

Results Our vaccine utilized hematopoietic stem cells obtained from human bone marrow-derived mononuclear cells (MNC). Through the proliferation and differentiation of hematopoietic stem cells using various types of cytokines, a large number of DCs that could be used in DC vaccines were obtained. The cells obtained were at least 60 to 330 times larger than the initial cell count. Through FACS analysis, CD141 were expressed in cDC1 were recognized to be highly expressive. Additionally, secretion of IL-12 and IFN-γ, which are cytokines related to the immune response of DC. It was also confirmed through CTL Assay that T cells showed killing ability against tumor cells showing WT1 expression by DC in vitro. Moreover, when the DC vaccine was used with PD-1 and PD-L1 inhibitors, it was confirmed that the tumor microenvironment was controlled, and higher cancer cell apoptosis was exhibited.

Conclusions We unveiled that solid cancer cells can be eradicated using the DC vaccine we developed with PD-1 and PD-L1 inhibitors.

Trial Registration IIT (Investigaor initiated trials) ready only

Ethics Approval Ready only

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