P3-021 NT: Immunotherapy/Vaccines Posters, Wed, Sept 5 – Thur, Sept 6

Dendritic cell vaccine in murine lung cancer model: comparison of monocyte-derived DC and stem cell derived-DC

Lee, Seog Jae[1] Kim, Myoung Joo[2] Baek, Soyoung[2] Kim, Hyun Soo[3] Lee, Hyunah[4]

[1] Eulji University, School of Medicine, Seoul, Korea [2] Samsung Medical Center, Seoul, Korea [3] Stem cell Institute, FCB-Pharmicell Co Ltd, Seoul, Korea [4] Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: Although anti-tumor effect of monocyte-derived DC (M-DC) vaccine was studied in several tumor models with feasible responses, the major huddle is yield of therapeutic cells in culture. Hematopoietic stem cell-derived DC (S-DC) was introduced as alternatives. In this study the in vivo anti-tumor effect of M-DC & S-DC was compared as well as the DC characters.

Methods: Syngeneic Lewis lung carcinoma cells (LLC) were inoculated intravenously into C57BL/6 mice to simulate the minimal residual disease (MRD). M-DCs were cultured from myeloid lineage cells negatively selected from bone marrow cells by antibody panning. Selected cells were cultured with GM-CSF and IL-4 for 6 days. Mouse bone marrow stem cells were isolated by MACS lineage cell depletion kit and cultured with GM-CSF, SCF and IL-4 for 13days. Tumor antigen pulsing was performed with autologous tumor cell lysate. Antigen pulsed therapeutic-DCs were injected twice by one week interval into the peritoneum of mice that are inoculated with LLC one day before the DC injection. Cultured therapeutic-DCs were characterized by phenotype and cytokine production nature. Anti-tumor responses and the immune modulation were observed 2 weeks after the final DC injection. Pulmonary tumor burden as well as tumor antigen specific lymphocyte proliferation (CFSE assay) and IFN-r secreting CD8+ T cell proportion (ELISPOT) were detected from the splenocytes of mice in each group.

Results: Both M-DC and S-DC vaccine treatment inhibit the tumor growth in the lung. Especially anti-tumor response of tumor lysate pulsed DCs (LDCs) were significant compared to saline treated mice. Over 90% M-DC & S-DC were expressed MHC I/II molecules. Interestingly, less than 10 % of M-DCs express CD11c but about 45 % of M-DCs express CD11b. S-DC expresses CD11c in about 80% of the cells especially CD11c+CD8a+ proportions were about 35% in S-DC but less than 2% in M-DC. IL-12 secretion was higher in S-DC (424.82+87.26 pg/106 cells) than in M-DC (73.51+6.15 pg/106 cells), but the secretion of IL-10 was higher in M-DC (65.99+4.30 vs. 180.70+18.99 pg/106 cells for S-DC vs. M-DC respectively). Induction of tumor antigen-specific lymphocyte proliferation was only observed in M-DC/LDC treated group (2.6% vs. 60.5% proliferating cells by media vs. tumor lysate stimulation in vitro). However the frequency of IFN-r secreting CD8+ T cells were in S-DC treated group was significantly higher than that in M-DC treated group (58.7+8.3 vs. 11.7+1.8 spots for S-DC/LDC vs. M-DC/LDC treated group, respectively).

Conclusion: Although the characters of M-DC and S-DC were different, anti-tumor effect of DC vaccines was similar in LLC MRD model. Tumor antigen specific lymphocyte proliferation was significant in M-DC treated group, however as a effector cells the frequency of IFN-r secreting CD8+ T cells were higher in S-DC treated group than in M-DC group. Conclusively, data suggested that S-DC might be better module as anti-tumor vaccine than M-DC in both yield and function.

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Role of Cadi-05 as an adjuvant therapy in advanced Non Small Cell Lung Cancer

Pant, Mohan C.[1] Chakraborty, B. S.[2] Patel, N.[2] Bisht, Shyam S.[3] Verma, Ved P.[3] Singh, Sharad[3] Gupta, Deepak[3] Gupta, Seema[3] Shah, Parag P.[4] Pant, Rajeev[5]

[1] KGMU, Lucknow, India [2] Cadila Pharmaceuticals, Ltd., Ahemdabad, India [3] Dept. of Radiotherapy, KGMU, Lucknow, India [4] Industrial Toxicology Research Centre, Lucknow, India [5] LCI, Lucknow, India

Background: Cadi-05 has been undergoing evaluation in management of cancers. This double arm, controlled phase II study was undertaken to evaluate safety & efficacy of Cadi-05 when used along with chemotherapy (Cisplatin plus Etoposide) for advanced stage Non Small Cell Lung Cancer (NSCLC).

Methods: Between January 2005 to June 2005 53 patients were randomized to one of the treatment groups. Patient in Group A received Cisplatin and Etoposide (CE) along with intradermal administration of Cadi-05 (Mycobacterium W-0.5 x 109 cells/ml) 0.1 ml fortnightly for a period of 6 months & patients in Group B received Cisplatin and Etoposide. All the patients were required to complete 6 cycles of chemotherapy.

Results: Of the 53 patients who were enrolled, 48 patients were eligible for final analysis; 26 in group A & 22 in group B. Patients in Group A had a median survival of 11 months and patients in Arm B had a median survival of 7 months. One-year survival rates were 46.2% for Arm A and 36.4% for Arm B. Response rate was 38% in group A and 27% in group B (see table 1). The most prevalent hematological toxicities were neutropenia, leucopenia, and anemia, which were slightly less in the group A (13%, 5%, 4% resp) than in the group B (18%, 10%, 5% resp.). Common non hematological toxicities in both the group were asthenia, anorexia, vomiting and dyspnoea incidence of which were significantly lesser in group A (21%, 13%, 8%, 7%) than in the group B (28%, 20%, 16%, 13% resp.) Patients in Group A tolerated the chemotherapy better, which resulted in higher compliance rate.

Conclusions: Higher compliance rate was observed in patients receiving Cadi-05. It improves response rate & median survival when administered as an adjuvant with chemotherapy containing Cisplatin plus Etoposide.

TABLE 1: Response rate

	Responders	Non Responders	
Group A	10 (38%)	16 (61.3%)	26
Group B	06 (27%)	16(72.4%)	22
Total	16	32	48