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Phase I clinical trials for the PD-1/MUC1 CAR-pNK92 immunotherapy**Leiming Xia**

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Mucin1 (MUC1), as an oncogene, overexpressed in many human carcinomas and plays a key role in the progression and tumorigenesis. MUC1 specific chimeric antigen receptors (CARs) modified T/NK cells has been shown to be an effective approach for inducing MUC1⁺ tumor cells death. However, treatment failure with CAR-T/NK therapy was usually caused by the high expression of negative immune-regulatory molecules in tumor microenvironment. PD-L1 has been identified as negative checkpoint molecules that promote immune evasion of tumor cells. The interaction of PD-1 and PD-L1 inhibits the function of tumor-infiltrating lymphocytes or infused T/NK cells while activating the negative immune-regulatory cells in tumor microenvironment. To conquer these barriers and transform the PD-1/PDL-1 suppression effect into a positive regulation, we engineered clinically applicable NK-92 cells by lentiviral gene transfer to express two kinds of chimeric antigen receptors (CARs) comprising an anti-MUC1 or anti-PDL1 scFv antibody fusion protein with CD28-CD137 as a signaling moiety and truncated PD1 peptide. Anti-MUC1-CAR expression by gene-modified NK92 cells specifically and efficiently lysed MUC1 positive tumor cells *in vitro* and *in vivo*. In this study, 10 patients with different kinds of tumor (lung cancer, pancreatic cancer, colon cancer and ovarian cancer) were enrolled with PDL-1 and MUC-1 positive through pathological examination, then CAR-NK cells were infused several times into the patients (1×10^9 cells total). Of 10 patients, 2 patients were withdrawn, 7 patients (70%) showed stable disease and 1 patient (10%) showed progressive disease. We also monitored the cytokines level and hematological changes to evaluate the safety. Most patients didn't shown cytokine storm or bone marrow suppression obviously. From these patients we found that CAR-NK therapy has a broad prospect of application as a novel immunotherapy related to its certain clinical effects, mild side effects and easy preparing. CAR-NK would play more obviously anti-tumor efficacy through Bi-target treatment.

Biography

Yangyi Bao has her expertise in evaluation and passion in improving the health and wellbeing. Her open and contextual effort on clinic of hematology and oncology has obviously promotes the treating level. Recently she conducted several clinical trials which use novel chimeric antigen receptor T/pNK cells targeting hematologic and solid tumors.

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