

POSTER PRESENTATION

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Vaccination with bispecific antibody armed T cells (BATC) in metastatic breast cancer patients and transfer of anti-breast cancer immunity in primed T cells after stem cell transplant: a proof of principle study

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Background

Despite improvements in treatment options, metastatic breast cancer (MBC) remains an incurable disease. In our recent Phase I immunotherapy (IT) trial in 23 women with MBC, 8 infusions of activated T cells (ATC) armed with anti-CD3 x anti-HER2 bispecific antibody (HER2Bi) given in combination with interleukin-2 (IL-2) and granulocyte-macrophage colony stimulating factor (GM-CSF) induced specific anti-breast cancer (BrCa) cytotoxicity and increased IL-12 and Th₁ cytokines in the serum¹. This study investigated whether specific cellular and humoral anti-BrCa immunity is induced by infusions of HER2Bi bispecific antibody armed T cells (BATs) could be transferred after high dose chemotherapy (HDC) and stem cell transplant (SCT).

Methods

T cell were activated with OKT3 and expanded in IL-2. ATC were harvested, armed with HER2Bi, and cryopreserved in 8 doses for twice weekly infusions for 4 weeks along with IL-2 and GM-CSF. Seven to 14 days after the last infusion of BATs, the patient was leukapheresed to obtain immune T cells. Immune ATC were harvested and cryopreserved for multiple infusions after the HDC and SCT. Cellular and humoral immune responses were monitored up to 24 months.

Results

Six of 8 MBC patients enrolled in the protocol, completed the protocol and were evaluable for transfer of cellular and humoral immunity. No dose-limiting events for the infusions, delays in engraftment, and life-threatening infections were observed. Five of 6 evaluable patients exhibited increased anti-BrCa cytotoxicity and IFN- γ Elispots after vaccination with BATs and up to 12 months post SCT. Serum and culture supernatants from *in vitro* antibody synthesis assay showed gradual increases in anti-SK-BR-3 IgG levels after SCT. Serum cytokine profile showed increases in IL-12 and Th₁ cytokines. One of 6 evaluable patients who rapidly progressed showed poor immune responses (CTL and IFN- γ Elispots), had high serum levels of Th₂ cytokines and no evidence of transfer of immunity. Flow cytometry analysis of V β repertoire pattern in PBMC collected post IT and post SCT indicate transfer of the major V β clones post SCT.

Conclusions

This pilot study suggests that optimal adoptive transfer of cellular and humoral immunity induced by BAT infusions using *ex vivo* expanded immune anti-breast cancer T cells after SCT accelerates not only immune reconstitution but, more importantly, enhances reconstruction of anti-tumor cellular and humoral immunity after HDC and SCT to achieve maximal tumor reduction and regulatory T cell ablation.

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1. Lum LG, Thakur A, Al-Kadhimi Z, Colvin GA, Cummings FJ, Legare RD, *et al.*. *Clin Cancer Res* 2015, **21**(10):2305-2314.

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