

POSTER PRESENTATION

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Adoptive immunotherapy with engineered T cells expressing and HLA-A2 restricted affinity-enhanced TCR for LAGE-1 and NY-ESO-1 in patients with multiple myeloma following auto-SCT

Aaron P Rapoport^{1*}, Edward A Stadtmauer², Dan T Vogl², Brendan Weiss², Gwendolyn K Binder-Scholl³, Dominic P Smethurst³, Jeffrey Finklestein⁴, Irina Kulikovskaya⁴, Minnal Gupta⁴, Joanna E Brewer³, Alan D Bennett³, Andrew B Gerry³, Nick J Pumphrey³, Helen K Tayton-Martin³, Lilliam Ribeiro³, Ashraf Z Badros¹, Saul Yanovich¹, Gorgun Akpek¹, Naseem Kerr², Sunita Philip¹, Sandra Westphal¹, Levine L Bruce^{2,4}, Bent K Jakobsen³, Carl H June^{2,4}, Michael Kalos^{2,4,5}

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We report on a 26 patient phase I/II clinical trial (NCT01352286) to investigate the safety, feasibility and anti-tumor activity of T cells engineered to express an affinity-enhanced TCR that recognizes the NY-ESO-1/LAGE-1 peptide complex HLA-A*0201-SLLMWITQC. Patients with high risk or relapsed, NYESO-1 and/or LAGE-1 positive multiple myeloma (MM), are infused with $1-10 \times 10^{10}$ autologous TCR-engineered T cells 2 days after autologous stem cell transplantation (aSCT). CD25 depleted CD4/CD8 T cells are activated and expanded by anti-CD3/28 beads, and modified by lentivector. Disease response is evaluated in accordance with IMWG criteria. Blood and marrow is monitored for the persistence and phenotype of engineered cells; marrow is monitored for expression of target antigen. 20 patients (average age of 57) were infused with an average of 8.7×10^9 T cells (range $4.5 \times 10^8 - 4.2 \times 10^9$), transduced at an average of 34% (range 18% - 49%). Patients received a median of 2 prior therapies including 6 with prior transplant. 50% of tumors contained high risk chromosomal abnormalities, and NY-ESO expression is correlated with adverse prognosis. Patients with disease just prior to transplant (14/17) were assessed for response by day 100 (Table 1). Infusions were well tolerated with no cardiac-related toxicity. At least possibly related grade 3/4 events included blood and marrow or GI

Table 1

| Best Response – D100 | # Pt | % |
|----------------------|------|-------------|
| CR | 1 | 7% (1/14) |
| nCR | 10 | 72% (10/14) |
| VGPR | 0 | 0 |
| PR | 3 | 21% (3/14) |
| SD | 0 | 0 |
| PD | 0 | 0 |
| Total | 14 | 100% |

toxicity, all of which resolved. Engineered T cells expanded and persisted in blood and marrow at 180 days by Q-PCR and flow-cytometry in all but one case. 7 patients progressed after day 100, which was accompanied by loss of engineered T cells or loss of tumor antigen. The response by day 100 compares favorably to historic responses in patients undergoing first or second transplant, which is encouraging in this advanced stage population. We are investigating correlates of response and mechanisms of relapse.

Authors' details

¹The Greenebaum Cancer Center, University of Maryland, Baltimore, MD, USA. ²Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. ³Adaptimmune Ltd, Oxford, UK. ⁴Department of Pathology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. ⁵Translational and Correlative Sciences Laboratory, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA.

¹The Greenebaum Cancer Center, University of Maryland, Baltimore, MD, USA
Full list of author information is available at the end of the article

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